Yale University

OFFICE OF THE PROVOST
New Haven, Connecticut 06520

September 29, 2008

VIA FEDERAL EXPRESS

Michael A. Carome, M.D.
Captain, U.S. Public Health Service
Office of Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Dear Dr. Carome:

I am pleased to submit this response on behalf of Yale University to the Office of Human Research Protections' (OHRP, the Office) request for information and comments regarding human subjects protection training and education programs. (73 FR 37460) My Yale colleagues and I appreciate the opportunity to share our views on this important matter.

We understand that, based on OHRP's experience in compliance activities and on the advice of multiple advisory and regulatory bodies, OHRP believes that a number of individuals involved in the conduct and/or review of human subjects research have gaps in their knowledge about human subjects protections and suggests that these gaps may be symptomatic of inadequacies in institutional education and training programs. Accordingly, OHRP is seeking comment regarding the advisability of issuing additional OHRP guidance or seeking additional Health and Human Services regulation pertaining to such training and education programs.

We believe that research institutions have an obligation to protect human subjects participating in research, and, more specifically, we agree with OHRP that education and training programs are critical to institutions' success in meeting that obligation. That said, we feel there is an insufficient body of evidenced-based studies that 1) document the relation of deficiencies in specific features of education and training programs to instances of non-compliance; and 2) illuminate those educational measures that would be most effective in preventing non-compliance and improving human subjects protections. Accordingly, we feel that regulation regarding education and training would be premature and, in fact, could consume agency and institutional resources that could be more effectively deployed to other human subjects protections activities. Moreover, we urge that OHRP supplement and support any guidance on this matter with studies to measure the impact of educational and training programs on the effectiveness of human subjects protections programs and thereby assist institutions in identifying areas of vulnerability and opportunities for real improvement.

Yale University's Implementation of OHRP Training Recommendations

Yale University maintains a human subjects research education and training program that, as recommended in the terms of the Federalwide Assurance, includes all personnel who are involved in the conduct, review, and oversight of human subjects research, e.g., the Signatory Official; the Human Protections Administrator; Institutional Review Board (IRB) chairs, members, and staff; principal investigators; and research personnel named on research protocols (Question 1a). In accordance with this program, these personnel are required to complete basic training in human subjects protections by taking an on-line or face-to-face course in human subjects research protections provided by the University, taking courses provided by the National Institutes of Health (NIH) or the Collaborative Institutional Training Initiative (CITI), or by completing training that is deemed equivalent to that provided by the University, NIH, or CITI.

In addition to basic training, Yale provides additional orientation for new IRB members and regular educational updates for all IRB members during IRB meetings. A robust calendar of additional formal and informal educational offerings relating to ethical, regulatory, and administrative issues in the conduct of human subjects research is available to the entire Yale community and publicized through a number of venues including the Yale Interdisciplinary Bioethics Center.

Yale notifies the community of training requirements in human subjects protections and a number of other areas (e.g., conflict of interest, biosafety, sexual harassment, information security) and tracks compliance with these requirements through Yale-developed software, the Training Management System (TMS). Every faculty and staff member is asked to complete annually a TMS assessment profile that determines, based upon assessment responses as well as employment-related information, the types and frequency of required training. TMS also provides access to on-line courses and to registration for face-to-face training; issues certificates of completion; and maintains an on-line database of completed training, which can be accessed by faculty, staff, supervisors, and directors of compliance units.

Components of an Effective Education and Training Program

OHRP has asked institutions to comment on features of education and training programs that might be addressed in guidance or regulation. We believe that many of these features add value to an education and training program including:

- Inclusion of individuals involved in the conduct, review, and oversight of human subjects research (Question 2);
- Creation of a consistent level of basic, minimum training, meaningful for all participants in human subjects research, e.g., core ethical principles (Question 3a and Question 5);
- Customization of content for various roles and areas of research (Question 3b);
- Regular review and appropriate updating of content and curriculum (Question 3d);

- Expectations of periodic training for individuals with ongoing or recurrent involvement in human subjects research (Question 6); and
- Systems or procedures to ensure and document that individuals complete training (Question 7 and Question 8).

That said, we believe that these features can be developed and implemented most effectively when there is sufficient flexibility to tailor programs to accommodate the unique needs and circumstances of individual institutions and the diversity of personnel and research projects within those institutions. Accordingly, we recommend that OHRP guidance be stated in terms of objectives and desired outcomes instead of specifying how institutions should reach these objectives. It also would be useful for OHRP to make available to the research community a collection of best, as well as troublesome, practices identified in the course of OHRP reviews and enforcement proceedings.

As OHRP considers guidance regarding education and training, we hope the Office will bear in mind that training is but one component of a broader human subjects protections program and that enhancement of training is but one means to improve human subjects protections. All these components compete for institutional and agency resources, and increases in the scope of any one component may come at the expense of the others. Accordingly, we hope that OHRP guidance will focus upon those aspects of education and training that have been shown to provide substantial benefit to human subjects protections.

Thank you again for the opportunity to comment on this important issue.

Sincerely yours,

Stephanie S. Spangler, M.D.
Deputy Provost for Biomedical and Health Affairs

Cc: Maurice J. Mahoney, M.D., J.D., Executive Director, HIC
Sandra L. Alfano, Chair, HIC I

Carome, Michael A (HHS/OPHS)

From: Zuccarelli, Anthony (LLU) [azuccarelli@llu.edu]

Sent: Monday, September 29, 2008 10:51 PM

To: PSC Humansubjectstraining

Cc: Quick-Wolfe, Janice; Sarmiento, Lorraine (LLU); Halstead, Linda (LLU); Krausz, Jr (LLU)

Subject: Human Subjects Protection Training and Education

Comments on Human Subjects Protection Training and Education

(1a) This response is based on the perspectives of our institution only. We hold an OHRP-approved FWA and we have implemented OHRP recommendations on training and education.

(1b) Our institution has implemented OHRP recommendations for training and is currently engaged in a comprehensive review and expansion of its research educational program. Based on our experience, we believe that limited funding is often a key reason for delayed implementation of training recommendations. In an era of tight budgets, expenditures must be justified at multiple institutional levels. For example, when we proposed a research education coordinator position, our human resource management department required us to cite specific regulations mandating such a position. Since we receive National Institutes of Health (NIH) funding, we were able to use NIH requirements as justification. Substantial staffing costs are incurred to support educational recommendations, either to hire dedicated instructional personnel or to compensate existing administrators, educators, or investigators for assuming this additional responsibility. A second cost-driver is meeting the requirement to document and track training in a comprehensive way. Financial limitations obstruct software acquisition, such as Learning Management Systems (LMS), to assign training requirements to investigator categories, notify them of annual obligations, schedule training activities, and document fulfillment of educational requirements. At our institution, we are expanding our training offerings within the confines of existing systems, a challenge that requires a substantial investment of time and creativity. A federally mandated program, rather than the current method of government recommended and guided training, would represent a considerable unfunded mandate. It would come at a time when healthcare is stressed by decreasing reimbursement and federal grant funding is in decline.

(1c) We have not observed a failure of an institution to implement OHRP recommendations and, consequently, are unable to respond to this question.

(1d) This question presumes that a failure to accept and adapt OHRP training recommendations has been a significant factor in noncompliance with requirements for subject protection and lead to actual incidents of inadequate protection. Reality is more complex, but accepting the premise for the purpose of providing a response, we are confident that additional regulations would not be "the best mechanism to address this problem." Support for our conviction follows.

We assume that the goal of the proposed plan is to achieve greater protection for research subjects. That is the intended goal of current laws and regulations. Training and education are intuitively important for compliance with laws and achieving improved subject safety, however, there is considerable opportunity for a discontinuity between training and improved practice. One is an input, the other an outcome. Training is necessary, but not sufficient, for compliant performance and regulation of training is still further removed from subject safety. The ancient saying, "'Tis many a slip between the cup and the lip," pertains here. It would be extremely difficult to devise a federal regulatory scheme for training that, given the diversity of research contexts and institutions, would invariably result in improved subject safety. We genuinely believe that education and training that reflect local conditions and incorporate institutional values will have a greater positive effect on investigator compliance and subject safety.

It is useful to note that clinical trials involving investigational drugs and devices, which may represent the most serious risks to research subjects, are already are comprehensively regulated by the FDA. In response to that oversight, large pharmaceutical companies have generally assigned significant resources to training. Investigators and key personnel are routinely trained by the study sponsor on the subject protection. It seems unlikely that additional regulation would significantly improve what large pharmaceuticals have already accomplished with existing incentives.

Smaller device manufacturers, investigator-initiated and student research projects usually do not have access to the same level of resources. Since the rules and requirements are the same, the question is not whether training is important and useful, but whether an institution with limited resources, unique perspectives, and institutional insights, is in a better position to know what will be locally effective than a remote government agency.

2) If HHS proposed further guidance on training, from our experience, no particular group stands out as needing education more than another. Each group has a role to carry out in the process and must be informed of the implications of the decisions that are made. As stated previously, investigators for drug company-sponsored clinical trials seem to be trained more thoroughly. Nevertheless, it is difficult to document a high correlation between training time and improved performance or behavior. A regulatory scheme so detailed that it particularize the rules down to different groups or roles of individuals involved in research would be reaching even deeper into the structure and function of local institutions and conditions for control. No matter how well-intended, that option is rife with opportunities for missing the intended target. As an example, "old school" investigators are inclined to do things as they have for 30 years, in spite of training updates. Local understanding of the personalities, relationships with colleagues, and history with the institution are indispensable in crafting an education environment that will successfully reorient those entrenched attitudes. Externally formulated regulation can't do that, but will still consume institutional resources that could be used more effectively.

3a) Any potential further guidance or regulation should not include specific content for education and training programs since the institution is in a better position to make that determination. This, in fact, is the theme of this commentary.

3b) Each institution can decide their own requirements based on their observations and specific situations.

3c) It is reasonable to expect a minimum level of knowledge of research personnel, but how that training is organized and delivered should remain flexible.

3d) Some topics may not need to be updated often. Others may need to be changed periodically, especially if the underlying requirements (e.g., state or federal law) change.

4) The current requirements seem sufficient.

5) The current guidance seems sufficient.

6) We feel that each institution is in the best position to determine how often training should occur and the time intervals between training sessions. The institution should have flexibility in this area.

7) Guidance might be provided to recommend that institutions prepare and maintain written procedures, though implementing such tasks may place an excessive burden on institutions with limited administrative staff. Further, since education is typically not a "cookie-cutter" operation, the actual training program is likely to be an amalgam of online resource, live-classroom, book study, one-on-one mentoring, in-services, etc. This is difficult to document in procedures. They must either be written so generally as to provide little guidance, or consume huge resources to re-write as procedures catch-up to the "real-world" of what is happening in the institution. Since, as discussed earlier, institutions often lack dedicated funding for training, the effort to maintain documentation of training is also unfunded. At a minimum, a reliable source of funding for any additional requirements must be clearly stated.

8) Institutions should have the flexibility to determine what training requirements are needed and manageable since the institutions and their research vary greatly. Having mandated requirements does not seem appropriate.

9) Costs to an institution for implementing mandated training will be significant, especially if investigators' time is evaluated. For example, as a medium sized institution, we have approximately 3,000 investigators in our database who have received training recently. We have one FTE assigned to coordinate the educational program and we currently use CITI as the platform for our training. Next year, CITI will be charge $1,500 for their services, which is quite reasonable. However, theirs is not a full-service LMS, so we have to manually enter the data received from CITI into a local database to track training requirements and activities. If educational requirements are not met, the study must be put on hold until they are satisfied. Though this is an effective compliance mechanism, it is consumes considerable staff time and effort because CITI does not directly communicate with our database (manual entry is required) and the database does not automatically inform investigators of their educational status. Our goal is to expand research training university-wide, beyond human subject protections, to grant requirements, time and effort recording, conflicts of interest,

financial responsibilities, export controls, etc. In addition to the CITI online modules, we have regular live meetings for clinical coordinators and department administrators to discuss grant and contract issues. Training enforcement (suspending studies), routine training meetings, and live training sessions occupy at least 1.5 FTEs. Because of the caliber of personnel required, these tasks cost $150,000 yearly in salaries and benefits. Software purchases and licenses, programming, national workshops and training sessions for staff are additional costs. Significant new requirements may require an additional 0.5 FTE and force us to purchase a LMS system. Investigators' time must be considered as a real cost, especially if new mandates are contemplated. Based upon our current activities, a modest estimate of the annual cost of our research training program is given below.

Personnel costs 1.5 FTE	$150,000
Investigator time basic ($50 x 4.5 hrs x 500 trainees)	112,500
Refresher course ($50 x 1 hr x 2000 trainees)	100,000
IRB continuing education ($75 x 1 hr x 40 members)	3,000
CITI	1,500
Software purchases, upgrades, licenses	5,000
Workshops & training for staff IRB ($1800 x 1.5 meetings x 6 staff	16,200
Total annual cost	$388,200

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Carome, Michael A (HHS/OPHS)

From: Liz Wool [lizwool@qd-qts.com]
Sent: Tuesday, September 30, 2008 1:05 AM
To: PSC Humansubjectstraining
Subject: Request for Information and Comments on the Implementation of Human Subjects Protection Training and Education Programs.
Attachments: OHRP PUblic Comment_Education and Training _27 Sept 2008_lwoolqd-qts.com.pdf; Wool.pdf

Good day,
I forgot to add my answers to the specific questions posed by OHRP in the request for public comment.

As it is still 9/29/08 here on the west coast, I hope that you will accept this document.

Thank you!
Liz

Liz Wool, RN, BSN, CCRA, CMT
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27 September 2008

Office of Human Research Protections
Public Comment: Human Subjects Protection Training and Education

To whom it may concern:

In the last decade, clinical researchers have conducted clinical trials whereby their lack of knowledge of human subject protections embodied in Good Clinical Practices and ethical conduct for research (Belmont Report, Declaration of Helsinki) has resulted in clinical trial misconduct and subject deaths. Notably, these cases were reported in both our news media and professional publications. These cases, Jesse Gelsinger (1999, University of Pennsylvania, Gene Therapy Program) and Ellen Roche (2001, Johns Hopkins Hospital) were inspected by both the FDA and the Office of Human Research Protections (OHRP) with the identification of a broken system of clinical research oversight and human subject protection. These findings document that our 'System of Shared Responsibilities' was gravely broken at these institutions. Granted, since these occurrences, these issues have been addressed by both institutions, however, the 'broken systems' could have been prevented with proper training on human subject protections, GCP training and additional topics. Since these landmark events, clinical researchers continue to not understand their responsibilities and how to implement these responsibilities in clinical trials hence we continue to see institutional and investigational site regulatory inspections identifying significant issues in the conduct of clinical research.

Establishing mandatory training for clinical research does have precedent in both US based medical practices and the US product development regulations. Firstly, in the US Code of Federal Regulations, training and training documentation is a requirement in both Good Manufacturing Practices (21 CFR 201 and 210, QSR) and Good Laboratory Practices (21 CFR 58) for the activities and personnel employed in these non-clinical specialties. It is now time to bring the same level of requirements, standards, and performance to the GCP arena, which is much closer to ensuring subject safety than the production of investigational products and animal studies. Secondly, as a Registered Nurse, my nursing school training was multi-tiered before I was allowed to take a patient's vital signs, administer a medication, administer shots, perform venipunctures and taking a patient's intake history for their medical record. This training including the following:

1. Read about the patient's disease, disease diagnosis methods, disease treatments (medications, other therapeutic measures), potential side effects of medications and any treatments.
2. Verbally discuss with the nursing instructor the above in relation to the patient's presenting disease, as well as, concomitant illnesses and concomitant medications. This also included a requirement to understand drug-drug interactions as well.

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3. Observing the performance of a therapeutic intervention, prior to performing my doing it alone (e.g. skin ulcer dressing changes, giving a shot etc.). I would have to explain, in detail, the rationale for the intervention, potential negative consequences if not performed correctly, any specific precautions to take, and a step-by-step description of the intervention I was being trained on.
4. Perform the nursing/therapeutic intervention with the nursing instructor observing me. The nursing instructor would document that I was 'qualified' to perform the specific therapeutic intervention independently.
5. Lastly, I had to pass the 'nursing board examination' to be a registered nurse and nurses are required to maintain their 'currency' with nursing and medical practice as evidenced with the continuing education requirement linked to nursing license renewal standards.

Therefore, clinical researchers need to be approaching clinical trials, and the care of our study participants, the 'subject', as equal to medical practice and ensure that professionals designated to 'care for our subjects', are trained to the same standards as non-clinical research subjects (e.g. medical practice, clinics etc). Would a physician/PhD/dentist/nurse practitioner in private practice actually delegate these responsibilities to un-qualified staff per state licensure requirements and professional liability standards? I believe not. As a professional who has held positions as a Research Nurse, Clinical Research Associate (CRA), Clinical Trial Manager, as well as in Clinical Compliance – Standards and Training, and Clinical Research Training, I continue to be concerned at the inadequate knowledge and lack of practical training (how are staff trained to obtain informed consent, identify and report AEs/SAEs, perform study procedures, review an Investigator's Brochure for safety profile review, documentation etc), for institutions, IRBs, investigators, sub-investigators, study coordinators and study personnel ranging from stand alone private practices to academic institutions.

In the training of our health care professionals, the educational approach includes self-study, classroom learning and on-the-job-training. However, with the emergence of on-line/e-learning/computer based training, many people believe that completion of such learning modules state that they are trained and qualified to conduct their role in clinical research. However, without the inclusion of on-the-job training, such on-line learning is merely the same as 'reading a textbook'. And, such a training practice for either a doctor or a nurse would not be viewed as resulting in a competent skill level for patient care (ie. qualified to care for the patient on the topic being 'read' online alone). As we move forward to guide the development of this regulatory requirement, I would like to strongly recommend that as the regulation is written, that OHRP take into consideration these requirements and most importantly 'on-the-job training' on specific topics and training documentation (i.e. training records) for deeming personnel 'qualified' to perform their assigned duties. (Wool, June 2008, *Monitor* magazine).

In closing, recommendations for training have been noted in the OHRP Determination Letters and FDA Warning Letters over the past few years (e.g. GCP, investigator responsibilities, adverse events, case histories, investigational product management and accountability, informed consent, staff training on protocol/study procedures, corrective and preventive actions for errors in research execution etc.). Requiring mandatory training for institutions, investigators, IRBs

and study staff engaged in clinical trials and under the purview of GCP can be substantiated and benchmarked to current requirements in the US CFR for GMP and GLP regulations as previously discussed. This level of regulatory requirement is needed as well in the GCP arena. Clinical researchers governed by GCP are actually 'closest' to the care of the study subject of all three of these specialties (GMP, GLP, GCP) so, why not then bring the training standards and requirements up to the same level as GLP and GMP?

Attached to this letter are specific answers to the OHRP questions for public comment.

I would be honored to be considered as a contributor to this regulation and the solutions for implementation 'in clinical research practice' as I am active in the clinical research industry (President, ACRP Northern California Chapter, DIA and SQA speaker, ACRP faculty, clinical research faculty positions at UC Berkeley, UC Santa Cruz, San Francisco State University, and program advisory board member UC Berkeley) and after 30 years in the healthcare profession and 18 years in clinical research, my passion is still strong to make a difference and be part of the solution!

Sincerely,

Liz Wool, RN, BSN, CCRA, CMT
President and CEO
QD-Quality and Training Solutions, Inc.

PART II

(2) If HHS decided to propose further guidance recommending, or a regulation requiring, that institutions implement training and education programs for certain individuals involved in the conduct, review, or oversight of human subjects research, which of the following categories of individuals should receive training and education and why: IRB chairpersons; other IRB members; IRB staff; principal investigators; others involved in the conduct of human subjects research (e.g., co-investigators, study coordinators); FWA signatory officials; human protection administrators; or any other category of individuals (please specify)? **ALL**

(3a) Should further guidance or a regulation include provisions stipulating specific content for the training and education programs? **YES**If so, what should the specific content include and why (for example, should a regulation require inclusion of any or all of the following in the content of the training and education programs: The commitments and responsibilities of the institution under the FWA; relevant ethical principles cited in the institution's FWA; relevant Federal regulations for human subjects protection; **OHRP** guidance; other applicable guidance; relevant state and local laws; institutional policies for the protection of human subjects; or other content (please specify))? **YES, per position, all of the above.**

(3b) Should the training and education recommendations or requirements differ depending upon the nature of the individual's involvement in research? If so, in what manner? **Standardized training plans and requirements per the individual's role and responsibilities.**

(3c) Notwithstanding whether training should be tailored according to an individual's role in the clinical research process, is there a minimum level of knowledge and skill that should be expected of anyone working in some aspect of the research enterprise? **Yes, ethics, GCP and technical skill for all aspects of clinical research responsibilities per the job requirements/job descriptions.**

(3d) How often should the content of the materials used for this training be updated? **Review annually and update accordingly. This is the quality systems standard that sponsors utilize for their activities.**

(4) Should further guidance or a regulation include provisions stipulating that proficiency in human subjects protection requirements be demonstrated in some way (please specify)? **Yes, per job requirements. PI – understanding and synthesizing IB information and development of informed consent, and the evaluation of the ongoing risk-benefit analysis for both his/her participation and subject enrollment. All staff – GCP and practical, tactical skills are exhibited (ae identification and reporting, SAE identification and reporting, maintaining case histories, informed consent etc).**

(5) Should further guidance or a regulation include recommendations or requirements for individuals to complete some minimum amount of training and education prior to any involvement in the conduct, review, or oversight of human subjects research?**Yes, on-the-job training,s how competency of theory and practical application and skill.**

(6) Should further guidance or a regulation include recommendations or requirements for periodic continuing training and education? If so, should the guidance or regulation stipulate a specific time interval for such periodic training and education (for example, should the

regulation require individuals to complete continuing training and education activities every 1, 2, or 3 years)? **Yes, annual GCP training.**

(7) Should further guidance or a regulation include recommendations or requirements for institutions to prepare and maintain written procedures for ensuring implementation of the training and education requirements? **Yes, SOP for employee training (1)training plans for each job/job function (2) individual employee training plan addressing regulations, procedures and on-the-job training (3) trainer qualifications (4) on – the – job trainer qualifications (5) define 'competent' to perform a specific job activity independent from their trainer.**

(8) Should further guidance or a regulation include recommendations or requirements for institutions to prepare and maintain written documentation that individuals covered by the regulation have completed the required training and education activities? **Yes, implement same requirements that GMP and GLP regulations require and standards that sponsors work with in the industry. Individual training plan, reviewed and updated annually and with new jobs/responsibilities are added to the plan. Please refer to ACRP June 2008 article, Good Training Practice 101: A Primer for Employee Training Plans (Wool)**

(9) If HHS decided to propose a regulation, what would the estimated costs of the regulation be to institutions in terms of infrastructure and man-hour costs?**The establishment of the quality management systems (procedures, training, QC measures, QA audites) will be a one-time charge. There will need to be a compliance standards and training function to manage development, deployment, implementation and process improvements, documentation and regulatory agency inspection support. Once implemented, it will be maintenance only and ensuring there is a QC and QA function in place.**

OHRP is interested in receiving specific information on such estimated costs from all types and sizes of institutions that hold **OHRP**-approved FWAs. **OHRP** recognizes that the HHS human subjects protection regulations extend to a wide-range of institutions, from very small organizations and businesses that employ no more than a total of 5-10 individuals, to major academic research and health centers that may have literally thousands of individuals affected by any new training and education regulation. When providing comments regarding cost estimates, please include a description of assumptions that were made for calculating cost estimated (for example, assumptions made regarding the number and types of individuals who would be required to undergo training and education, the modalities that would be used for delivering the training and education, the time it would take for covered individuals to complete initial and continuing training and education, and how often continuing training and education would need to occur). **Recommendation: Annual GCP training should be topical, and oriented to the issues at the institution and trends/patterns in GCP activities. This can be a standard topic offered via classroom, webinar. Caution with on-line learning if it is not associated with practical, on-the-job discussions or training within department for 'relevancy' and assurance people are able to 'implement' the new knowledge. Many people do not learn via on-line learning.**

Carome, Michael A (HHS/OPHS)

From: SARENA D SEIFER [sarena@u.washington.edu]
Sent: Tuesday, September 30, 2008 9:26 AM
To: PSC Humansubjectstraining
Cc: Sarena Seifer
Subject: Human Subjects Protection Training and Education

Attachments: OHRP-Comments-092808.doc

OHRP-Comments-0
92808.doc (553 ...

Please see attached - this was originally sent at 3:30 pm EST on Monday September 28 and bounced back this morning as undelivered. I am trying again. Please confirm receipt. Thanks!

Sarena

****
Community-Campus Partnerships for Health promotes health (broadly defined) through partnerships between communities and higher educational institutions.
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Conference proposals are due October 10, 2008 - see www.ccph.info for details
****

Comments on the Implementation of Human Subjects Protection Training and Education Programs
September 29, 2008

Submitted by:
Education Network to Advance Cancer Clinical Trials (ENACCT) &
Community-Campus Partnerships for Health (CCPH)

Submitted to:
Department of Health and Human Services, Office of the Secretary, Office of Public Health and Science
Office for Human Research Protections

Background

The Education Network to Advance Cancer Clinical Trials (ENACCT) and Community-Campus Partnerships for Health (CCPH) are pleased to submit comments on the Implementation of Human Subjects Protection Training and Education Programs in response to the DHHS request. ENACCT is the only national organization devoted solely to identifying, implementing and validating innovative community centered approaches to cancer clinical trials education. CCPH is the only national organization devoted solely to promoting health through partnerships between communities and higher educational institutions, using community-based participatory research, service learning, broad-based coalitions and other strategies.

Together we are spearheading a national federally funded initiative, *Communities as Partners in Cancer Clinical Trials: Changing Research, Practice and Policy,*[1] which is exploring the potential of employing *community-based participatory research* principles and approaches to improve multi-site, phase III cancer clinical trials. Community-based participatory research (CBPR), as defined by the Federal Interagency Working Group on CBPR[2] and subsequently adopted by the NIH Scientific Interest Group on CBPR,[3] is "scientific inquiry conducted in communities in which community members, persons affected by the condition or issue under study and other key stakeholders in the community's health have the opportunity to be full participants in each phase of the work, including conception, design, conduct, analysis, interpretation, conclusions and communication of results." Our forthcoming national report[4], to be released in October 2008, makes a number of recommendations relevant to the issue of training and education of clinical research teams and IRB members, for which OHRP is seeking public comments and guidance. These are summarized below and worded to be broadly applicable to human subjects research.

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[1] Communities as Partners in Cancer Clinical Trials: Changing Research, Practice and Policy is funded by grant number 1 R13 HS016471 from the Agency for Healthcare Research and Quality, with co-funding from the National Cancer Institute. For more information, visit http://www.enacct.org/conference/conference.php

[2] Federal Interagency Working Group on CBPR. http://www.niehs.nih.gov/translat/IWG/iwghome.htm

[3] NIH Scientific Interest Group on CBPR. http://grants.nih.gov/grants/training/esaig/cbpr_sig.htm

[4] Education Network to Advance Cancer Clinical Trials (ENACCT) and Community-Campus Partnerships for Health (CCPH). (2008). *Communities as Partners in Cancer Clinical Trials: Changing Research, Practice and Policy.* Silver Spring, MD and Milwaukee, WI. Available on the ENACCT website at http://www.enacct.org and on the CCPH website at http://www.ccph.info

Comments

A. Need for additional guidance recommending that institutions engaged in human subjects research conducted or supported by the Department of Health and Human Services (HHS) implement training and education programs for certain individuals involved in the conduct, review, or oversight of human subjects research

We believe that additional guidance is needed to train and educate individuals involved in the conduct, review, and oversight of human subjects research. We believe this training needs to be required and needs to go beyond the content areas currently covered by the OHRP assurance training modules.

For those involved in the conduct of research (e.g., principal investigators, co-investigators, study personnel), we recommend that they be trained in these areas:

1. Engaging communities in research and optimal ways to integrate community members into research activities, including CBPR principles and approaches. This training should enable those involved in the conduct of research to:
    a. Develop mutually beneficial, sustained partnerships with existing community infrastructure, such as primary care providers and community-based organizations. These partnerships should engage in outreach and education efforts that inform the community about research beyond any particular study. Whenever possible, research sites located in the same geographic area should collaborate in these efforts.
    b. Engage in outreach activities with community groups, particularly those working to reduce health disparities, to educate the broader community about research beyond any particular study.
    c. Implement training for community members to prepare them sufficiently for the research related activities they will undertake.
2. Culturally and Linguistically Appropriate Standards and Clinical Trials (CLAS-ACT): Federal officials have recently underscored the need for cultural competency training in the research setting, supporting researchers to apply CLAS standards to the clinical trials process[5] and we agree. This training in cultural competency as it relates to study access, recruitment, and retention should enable those involved in the conduct of research to:
    a. Implement the consent process through trained staff, including, when available and appropriate, patient navigators who can assist in the consent process at the patient's request.
    b. Address the needs of minority, low-literacy, poor and elderly, underserved, and Limited English Proficiency (LEP) populations in the informed consent process, including the use of trained medical interpreters or a telephone language line[6] for LEP individuals, throughout the informed consent process and when consent forms are not available in the individual's native language.
    c. Appropriately use the OHRP-approved "short form" in the consent process.

For those involved in the review or oversight of research, (e.g., IRB administrators, members), we recommend that they have a basic of understanding of these issues, as applicable to the research application under review:

1. The disease being studied, including its standard of care.
2. The research process being proposed, be it traditional clinical research, CBPR, social and behavioral research, etc.
3. Key aspects of community outreach and accessible communication and education strategies.
4. The Belmont Report and ethical requirements for research.
5. The informed consent process.

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[5] Culturally and Linguistically Appropriate Standards And Clinical Trials. http://www.omhrc.gov/templates/content.aspx?ID=5046 and http://www.bcm.edu/edict/clas-act/index.htm

[6] 24-hour accessible interpretation services utilized in many health care institutions

For those involved in the review or oversight of research, (e.g., IRB administrators, members), we recommend that they be trained in these areas:

1. Strategies for community engagement in research, including CBPR.[7] While IRBs do consider the local context in which research is conducted, IRBs are neither expected nor required to assess the risks and benefits of a given study to participants' communities or the broader community, and most do not make this assessment.[8] Similarly, IRBs are neither expected nor required to assess the nature and extent of community support for the study. However, IRB examination of studies' community benefit and community support may improve overall research outcomes.[11]
2. Appropriate community member roles on the IRB.
3. How to consider evidence of community engagement in and community support for studies seeking IRB approval.
4. Approaches to appropriately address the needs of minority, low-literacy, poor and elderly, underserved, and Limited English Proficiency (LEP) populations in the informed consent process.
5. The appropriate use of the OHRP-approved "short form."

We also recommend that specific orientation, training and mentoring be provided for IRB community (non-affiliated, non-scientific) members to help ensure they are comfortable and competent in their roles on IRBs.[9] These members can help to ensure that language and other aspects of a research study make sense to the layperson. They can bring unique viewpoints to the IRB; nonaffiliated members are not biased by employment, and non-scientific members are not biased toward the research question.[10] They can play an important role in evaluating the benefits and risks to research participants, reviewing the informed consent process to ensure participant protection, reviewing protocols, and making presentations to community groups about the role of IRBs and the importance of human subjects research.[11, 12, 13]

There are a number of barriers to community members' participation on IRBs, including not having a clear definition and understanding of their role, and the complexity and amount of information reviewed.[14] Most, community IRB members, for example, view their role solely as simplifying consent forms.[15]

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[7] In January 2008, Community-Campus Partnerships for Health convened a workgroup to develop a CBPR training curriculum for IRBs and REBs. For more information, visit http://depts.washington.edu/ccph/irbhome.html or contact Jessie Tobin at jtobin@mcw.edu

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[15] Sengupta S, Lo B. (2003). The roles and experiences of nonaffiliated and non-scientist members of institutional review boards. *Academic Medicine.* 78(2):212-8.