Carome, Michael A (HHS/OPHS)

From: Nick Eastmond [neast@cc.usu.edu]
Sent: Monday, September 29, 2008 3:55 PM
To: PSC Humansubjectstraining
Subject: Human Subjects Protection Training and Education

Attachments: IRB_Article_Response8_08.doc; ATT969611.txt


IRB_Article_Respon se8_08.doc (...


ATT969611.txt (4 KB)

Dear Dr. Carome:

I am inserting my comments (1) as a text, below; and (2) as an attached file. I hope that these statements can be of help to your group.

Nick Eastmond

Utah State
UNIVERSITY

DEPARTMENT OF INSTRUCTIONAL TECHNOLOGY
College of Education and Human Services
2830 Old Main Hill
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Telephone: (435) 797-2694
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August 19, 2008
(Posted 29 September 2008)

To: Dr. Michael Carome, MD., Captain
US Public Health Service, ORHP

Fr: Nick Eastmond, PhD.
Professor

Subj: Response to proposal for new regulation or required IRB training

I read the lead article in your newsletter (Human Subjects Report), entitled "Major Proposal on the Protection of Human Research Participants" with some interest. I felt that I should comment, per your request.

I have recently started my involvement on our institution's IRB, and will be attending my first meeting next month. I have taught both beginning and advanced research courses at the graduate level in education where obtaining IRB certification was required for our students. I have also served on the Professional Ethics Committee of our professional association, the Association for Educational Communications and Technology, for the past 23 years. I recognize that the dangers associated with the field of education have considerably fewer hazardous consequences than those of the biomedical field, for example, at least in the short run.

If our institution is any indication, the compliance with IRB training, certification and research proposal approval represents a "sea change" for the institution. Considerable effort goes into obtaining IRB approval for a variety of research proposals, from certain student projects done for a single class to class projects to dissertation research to faculty grants for funded research projects. This kind of thought and scrutiny was unheard of in the past. There is a huge spectrum of projects now considered under these guidelines. I suspect that these changes are having an impact on the welfare of humans who participate in research, and I trust that the overall impact is positive.

I read with interest the portion of the article entitled "Cost factor is complex." It appeared to me that any current estimates of cost involved are purely estimates at this time. From my observations at this institution, the costs in personnel time in dealing with the current regulations are substantial. I would ask that you consider:

• How can it be that increased training in IRB procedures (from 1 hour to 4 hours for the basic certification at our school) can not have reduced the complexity of the application process or the amount of time required for proposal approval? Some kinds of class projects are almost impossible to start in the semester and complete 16 weeks later, due to the huge delay commonly encountered in obtaining IRB approval.

• How can the IRB and the entire institution develop a nuanced set of filters, so that projects that really entail risks to human subjects can be labeled and cautionary action taken, while the others can be expected to be handled intelligently by well trained faculty and students, now sensitized because of the required IRB training?

• What kinds of checks are made to insure that IRB work does not "clog up the system" and "deflect excellent research questions into mediocre but more easily approvable ones?"

As you can see, I am beginning my work on this committee with a set of concerns, many of which have been expressed in this letter. My final advice to your office is: Give time for education of the parties involved and work for ways that they can "learn the correct principles and govern themselves," rather than expanding the requirements or requiring additional training. And simplify whenever possible.

Thank you for soliciting this input. I hope that it can be of some help to you.

Sincerely,

Nick Eastmond, PhD.
Professor

ATT969611

August 19, 2008

(Posted 29 September 2008)

To: Dr. Michael Carome, MD., Captain

US Public Health Service, ORHP

Fr: Nick Eastmond, PhD.

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As you can see, I am beginning my work on this committee with a set of concerns, many of which have been expressed in this letter. My final advice to your office is: Give time for education of the parties involved and work for ways that they can "learn the correct principles and govern themselves," rather than expanding the requirements or requiring additional training. And simplify whenever possible.

Thank you for soliciting this input. I hope that it can be of some help to you.

Sincerely

,

Nick

Eastmond, PhD.

Professor

Carome, Michael A (HHS/OPHS)

From: Wilenzick, Marc B. [Marc.B.Wilenzick@pfizer.com]
Sent: Monday, September 29, 2008 4:04 PM
To: PSC Humansubjectstraining
Subject: Human Subjects Protection Training and Education
Attachments: FDA Draft Information Sheet Guidance.pdf

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

Re: OHRP Human Subjects Protection Training & Education

Dear Captain Carome,

Attached please find our comments to OHRP's July 2, 2008 *Request for Information and Comments on the Implementation of Human Subjects Protection Training and Education Programs.*

We have submitted our comments to both OHRP and FDA, which has its own docket, for consideration.

Thank you for the opportunity to provide input to your efforts to improve human subject protection.

Sincerely,
Marc Wilenzick
Assistant General Counsel
Pfizer

Pfizer Inc
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Tel 212 733 4210 Fax 646-383-9249
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Marc B. Wilenzick
Assistant General Counsel

September 29, 2008

http://www.regulations.gov
Jeffrey Shuren, MD, JD
Associate Commissioner
U.S. FDA, Division of Dockets Management
5630 Fishers Lane, Room 1061 (HFA – 305)
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humansubjectstraining@hhs.gov
Michael A. Carome, MD
Captain, U.S. Public Health Service
Office of Human Research Protection
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Re: FDA Draft Information Sheet Guidance [Form 1572];
Docket No. FDA-2008-D-0406 &
OHRP Human Subjects Protection Training & Education

Dear Commissioner Shuren and Captain Carome,

Pfizer, a research-based pharmaceutical company, submits these comments in response to the Food and Drug Administration's ("FDA") Notice of July 29, 2008 (regarding the D*raft Guidance for Sponsors, Clinical Investigators and Institutional Review Boards on Frequently Asked Questions – Statement of Investigator (Form FDA 1572)* and the Office of Human Research Protection's ("OHRP") July 2, 2008 *Request for Information and Comments (on the Implementation of Human Subjects Protection Training and Education Programs).* We thank you for the opportunity to offer comments on the proposals from the regulatory agencies, responsible for oversight of human research, within the Department of Health and Human Services ("the Department").

In its July Guidance, FDA notes that there are no minimum requirements for investigators participating in FDA regulated clinical trials. Such investigators must however be "qualified" to conduct the study and have "familiarity" with Human Subject Protection (HSP) and Good Clinical Practice (GCP) requirements. OHRP asked, in its notice of July 2, for comment on the minimum levels of knowledge and skill that should be required of investigators and study staff

(conducting clinical trials at OHRP regulated institutions) and whether regulation or guidance on HSP education and training is needed.

Background

FDA and OHRP do not provide comprehensive GCP or HSP training for investigators, study staff, or IRB members, or guidance on assessing the qualifications of investigators and study staff. With regard to members of Institutional Review Boards (IRBs), who are also directly responsible for HSP, IRB members are not required to have had training on or proficiency in research ethics, HSP or GCP. Instead, FDA and OHRP regulations require that the IRB, as an entity, have members with scientific and non-scientific expertise, varying "backgrounds," "experience and expertise", and "diversity and sensitivity". *See* 21 CFR 56.107; 45 CFR §46.107. With regard to GCP, FDA rules apply to the qualifications of the principal investigator, 21 CFR 312.53, ignoring the importance of the experience, qualifications, and training of other research participants (sub-investigators, IRB members, research coordinators, etc.) with regard to ensuring GCP and HSP. Lists of debarred, disqualified, and restricted investigators are published by FDA. FDA does not maintain a list of qualified or registered investigators, qualified or registered research centers, or qualified or registered research coordinators.

Accordingly, since medical schools (and similar training programs for medical professionals) seldom cover GCP or HSP requirements, researchers are reliant, in large part, on their institutions and research sponsors to provide and ensure appropriate HSP and GCP training.

Discussion

The challenge of improving researcher (and other study professionals') knowledge of HSP concepts and GCP is complicated by the different regulations and differing guidances put forth by ORHP and FDA, despite sharing the same conceptual framework (e.g. informed consent, IRB review, benefit-risk maximization, and compliance with written standards, study protocols, and SOPs). It is also complicated by the heterogeneity in biomedical research (interventional studies vs. observational studies, research with healthy volunteers vs. patients, research with vulnerable populations, etc.) and by fact that many trials include sites outside the U.S.

Research sponsors are expected to select qualified investigators and study staff and ensure that they have been or will be properly trained about the study, GCP, and HSP. This presumes the existence of an effective system for assessing and/or training clinical trial investigators. FDA and OHRP can and should help in setting standards for such training, in partnership with subject matter experts in academia and industry, and with other research stakeholders. GCP and HSP training of research coordinators is also critical, as well as quality role-specific training for other research staff and IRB members.

GCP & HSP Training

While study sponsors and research institutions have and often develop their own HSP and GCP training to meet regulatory obligations, this is an inefficient, piecemeal approach.
We support the development of clear objectives for this type of training and propose that the regulatory agencies within the Department work together on the development of those

standards. Such standards would allow study sponsors and research institutions to more easily evaluate training platforms and make increased use of role-specific programs offered by trusted third-parties.[1]

Consensus standards for HSP and GCP training might start with a list of concepts that needs to be covered in role-specific training, in addition to the regulatory requirements. For example, IRB members should have training in how to review biomedical research and, to that goal, the training should cover key concepts, such as how to evaluate:

1. Whether the research is scientifically sound?
2. Whether the study design is appropriate?
3. Whether the risks of the research have been appropriately minimized?
4. Whether the benefit-risk ratio is reasonable, given the knowledge that may reasonably be gained by the research?
5. Whether the subject selection equitable?
6. Whether there are vulnerable patient groups targeted by the research, for which additional safeguards needed?
7. Whether the proposed informed consent is adequate?
8. Whether the research includes appropriate safeguards to protect patient privacy and confidentiality?

Training in concepts such as these, and greater use of case studies, may prove more effective than training which merely describes the regulatory obligations codified in the Code of Federal Regulations. The establishment of consensus standards could facilitate greater use of case study approaches to HSP and GCP training, and improve the effectiveness of such training.

Use of Trusted Third-Parties

FDA and OHRP should facilitate and encourage efforts by research institutions and sponsors to partner with professional bodies, associations, and other non-governmental organizations to train investigators, clinical research coordinators and study staff, and IRB members. This would further the Agencies' goals of ensuring data integrity and patient safety. Specifically, we believe that research sponsors and institutions are interested in working, with trusted third-parties, to improve the quality of GCP and HSP training.

If FDA and OHRP endorsed the use of trusted third party training programs or recognized this as a "good practice", these programs would be more readily used across the research spectrum.

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[1] Among others, existing training and certification programs include those offered by:

- the *Association of Clinical Research Professionals* (Training and Certification of Clinical Research Coordinators, Clinical Research Associates, and GCP training);
- *Academy of Pharmaceutical Physicians and Investigators* (Certified Physician Investigator Training);
- University of Miami and the Fred Hutchinson Cancer Research Center (*Collaborative Institutional Training Initiative* on Human Research Protection training for IRBs and researchers).

If these programs meet FDA and OHRP requirements for GCP and HSP training, the agencies should acknowledge this.

The need for study specific training about specific protocols would continue, but study sponsors could focus their training on the protocol, rather than the foundational GCP and HSP concepts.

Certification & Accreditation

FDA and OHRP should affirmatively support investigator and study staff certification. Participation in such certification systems, incorporating GCP and HSP training, should be entirely voluntary. However, FDA and OHRP could acknowledge the value of such certifications and make available, on their websites, a list of clinical investigators, clinical research coordinators, IRB members, and research professionals who have been certified. This would encourage the commitment of time and resources by research professionals in obtaining participating in the training necessary to obtain those certifications.

Accreditation is another opportunity for FDA and OHRP to support improvement in GCP and HSP training. Accreditation, like certification should be entirely voluntary. However, the Department's support for and acknowledgement of trusted third-party accreditation systems could substantially improve the training and mastery of GCP and HSP concepts and processes. FDA and OHRP should encourage and endorse voluntary accreditation systems for research institutions.

Recommendation

We propose that FDA and OHRP work together to establish unified standards for GCP and HSP training. FDA and OHRP should encourage the use of trusted third-parties for HSP and GCP training and should support voluntary certification and accreditation systems. FDA and OHRP should also develop a system to track clinical investigators, research coordinators, IRB members, and research staff who have completed recognized HSP and GCP training, as well as those who have been certified, and clarify that completion of such voluntary programs constitutes compliance with regulatory obligations for training in GCP and HSP.

Of note, the Clinical Trial Transformation Initiative lists credentialing and accreditation of clinical trial sites, to improve study start-up timelines, as a possible project.[2] That forum might be an effective group for OHRP and FDA to work with NIH and other stakeholders to develop a framework for training, certification, and voluntary accreditation programs with trusted third-parties.

Sincerely,

Marc Wilenzick
Assistant General Counsel
Clinical Trial Policy & Regulatory Law

[2] *See* https://www.trialstransformation.org/projects/priority-areas-for-ctti-projects/

cc: Ivor Pritchard, PhD
Acting Director
Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Rachel E. Behrman, MD, MPH
Associate Commissioner for Clinical Programs
U.S. FDA (Mail Stop HF-18)
5600 Fishers Lane
Rockville, MD 20857

Carome, Michael A (HHS/OPHS)

From: Beth Israel [Beth.Israel@asu.edu]
Sent: Monday, September 29, 2008 4:04 PM
To: PSC Humansubjectstraining
Subject: Human Subjects Protection Training and Education

ASU ARIZONA STATE UNIVERSITY
RESEARCH AND ECONOMIC AFFAIRS

September 29, 2008

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

RE: Human Subjects Protection Training and Education Programs, Request for Information and Comments

Dear Dr. Carome:

I am pleased, on behalf of Arizona State University (ASU), to submit these comments with reference to OHRP's "Request for Information and Comments on the Implementation of Human Subjects Protection Training and Education Programs."

We fully endorse the comments submitted with respect to this matter by the Council on Governmental Relations (COGR) and the Association of American Medical Colleges (AAMC), dated September 29, 2008.

ASU, like COGR and AAMC, shares OHRP's view of the importance of training and educational programs for individuals involved in the conduct, review or oversight of human subjects research and we have implemented processes and controls to ensure that this training and education occurs at ASU. However, ASU does not believe that a change in the regulations mandating training is necessary or appropriate at this time.

The background information provided in OHRP's Request for Information as a rationale for developing new regulation does not reflect the evolution of educational programs at ASU. ASU has had mechanisms and approaches to education and training in place since 1998. We have conducted seminars and workshops to train our investigators, researchers, students, Institutional Review Board (IRB) members and administrative staff to ensure the protection of human subjects. In addition, we have invested in the development of our professional staff and our human participant protection program as a whole.

Assurance through FWA

We support the existing approach of a recommendation from OHRP through the terms of the Federalwide Assurance (FWA) regarding education and we would discourage OHRP from promulgating additional regulations on the issue of human subjects protection training and education.

ASU does not believe that noncompliance with existing regulations necessarily reflects a lack of training. Compliance is achieved by means of a variety of factors including comprehensive training and the development of a culture of compliance within an institution. Even if OHRP were to issue regulations requiring training (which ASU strongly opposes), OHRP would be hard-pressed to regulate the adequacy of individual behavior, which must be instilled by the institutional commitment to compliance. This culture of compliance is achieved by providing adequate support to investigators, maintaining effective oversight and, finally,

holding individuals accountable for their performance. ASU believes that the existing structure is adequate in its reliance on the FWA's strong recommendations for training and education.

Scope & Content of Training

ASU agrees with OHRP that individuals involved in the conduct, review or oversight of human subjects research should know and understand their responsibilities and should receive initial training appropriate to their roles prior to any involvement in such research. However, due to broad variability in job categories and the responsibilities of involved individuals, any prescriptive requirements related to the content, frequency or adequacy of training would be impractical and unworkable.

ASU strongly opposes arbitrarily prescribed or recommended intervals for training programs. The exact methods for obtaining this training should remain flexible and include the federally provided on-line training options, training provided by institutions for their own faculty, staff and IRB members (whether on-line, in person, or a combination of the two, etc.), and attendance at regional or national training conferences, workshops, and programs.

Similarly, training regulations must recognize the distinctions between the soft-sciences and the natural sciences; a one-size for all approach most definitely does not fit all. There must be recognition, on the part of OHRP that some research areas that involve human subjects are of lower risk than others. The existing framework accommodates this flexibility and variability.

Increased Documentation

ASU believes that new regulations calling for written documentation of training completion or procedures for implementing training programs or monitoring the training of individuals involved in human subjects research are unnecessary. Furthermore, such additional requirements would add significant bureaucratic and unfunded record-keeping requirements without enhancing the protection of subjects. Current regulations requiring this training prior to the initiation of any research involving human subjects are sufficient; administrative requirements to verify such training already exist.

Cost of Compliance

The costs related to compliance with the Federal regulations governing human subjects research have increased exponentially since 1995. In the eight-year period between 2000 (the year the National Institutes of Health introduced its training requirement) and the present, ASU's budget for IRB-related costs has increased almost 300%. These costs are not recovered through our Facilities & Administrative (indirect) cost recovery because of the cap of 26% imposed by the Office of Management & Budget in 1995 and thus represent a true cost to the university.

A change in the regulations would, without question, result in substantial additional costs to ASU. The cost of implementation of any new regulations would be in addition to these already considerable expenses that ASU incurs in conducting human subjects protection training (and this is only one of many unfunded mandates imposed upon us). ASU would face these additional, unfunded costs at a time when, due to the stagnant NIH budget as well as economy in general, we are struggling to raise funds necessary to sustain teaching and research.

OHRP Contribution

ASU would welcome OHRP collecting and making available to all institutions links to "model" educational programs that have been developed by individual institutions. We would also welcome additional OHRP-developed training modules or, as COGR/AAMC suggested, if OHRP could recommend or provide mechanisms to fund the development of training tools and modules at the national levels.

Again, ASU is pleased to comment on the OHRP's Request for Information. We look forward to working with you on this topic in the future.

Sincerely yours,

Beth H. Israel

Beth H. Israel
Associate Vice President Research Administration

Beth H. Israel
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Carome, Michael A (HHS/OPHS)

From: Loess-Perez, Susan [SLOESSPE@depaul.edu]
Sent: Monday, September 29, 2008 4:22 PM
To: PSC Humansubjectstraining
Cc: Warren, Laura
Subject: Human Subjects Protection Training and Education

Attachments: 9-29-08 Letter to OHRP.pdf

9-29-08 Letter to OHRP.pdf (89...

To Whom it may concern,

Attached are comments from DePaul University regarding your request for comments on Human Subjects Protection Training and Education. We look forward to reading the summary resulting from your request when they are available.

Best regards,

Susan Loess-Perez, MS, CIP, CCRC
Director, Office of Research Protections Academic Affairs DePaul University
1 East Jackson Blvd.
Chicago, IL 60604

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DEPAUL UNIVERSITY

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September 29, 2008

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

Re: OHRP Request for Comments on Human Subjects Protection Training and Education Programs, Fed. Reg. Vol. 73, No. 127, pp. 37460-37463 (July 1, 2008)

Dear Dr. Carome,

On behalf of DePaul University, I would like to submit the following comments in response to the Department of Health and Human Services, Office for Human Research Protections' ("OHRP") Request for Information and Comments on the Implementation of Human Subjects Protection Training and Education Programs, published at Federal Register Vol. 73, No. 127, pages 37460-37463 (July 1, 2008) (hereinafter referred to as "Request").

Summary of Comments

DePaul University ("DePaul") believes that due to lack of awareness, many institutions have not routinely implemented OHRP's previous recommendations for human subjects research training. In response, DePaul recommends that OHRP issue additional guidance, rather than a regulation, requiring training and education for persons involved in human subjects research. This additional guidance should identify specific expectations and content for training and should establish a minimum regimen that must be completed prior to involvement in such research. In addition to baseline training, the guidance should also mandate some form of continuing education every three years, although attendance at professional association conferences should fulfill this criterion. To minimize the significant costs of implementing such guidance, DePaul recommends that OHRP sanction use of the Collaborative Institutional Training Initiative ("CITI") online training program. Finally, OHRP should encourage institutions to develop written policies and procedures for training and education requirements, including documentation of completion.

Beyond these requirements, DePaul believes that OHRP should accord institutions vast flexibility to tailor their training and education programs to their specific personnel and research portfolios. For example, institutions should be free to implement more stringent requirements for persons with the greatest responsibility in human subjects research design and conduct. To that end, OHRP guidance could identify additional training and education opportunities that are available, but remain optional, for key personnel. Institutions should also retain discretion when

deciding whether to update training materials and determining whether an individual has demonstrated proficiency in human subjects protection.

Comments on Questions in Request

In response to the questions presented in the Request, DePaul states as follows:

(1a) Have institutions holding OHRP-approved FWAs routinely implemented OHRP's recommendations?

It is our belief that many institutions have not routinely implemented OHRP's recommendations for human subjects research training, and those who have do not often mandate or prioritize the implementation of continuing education. In response to a National Institutes of Health ("NIH") policy developed in 2000, most institutions developed basic training requirements as a condition of receiving grant or contract funding. However, many institutions limited their requirements to initial education, as neither OHRP nor NIH require documentation of continuing education. Institutions that are knowledgeable about the FWA application process, either as a result of a visit from OHRP or through the accreditation process of the Association for the Accreditation of Human Research Protection Programs ("AAHRPP"), may understand that OHRP highly recommends continuing education related to human subject research for persons in particular positions. However, the person(s) preparing or filing the FWA often does not understand what is prepared and submitted to OHRP and does not realize that the FWA recommends both initial and continuing education. Moreover, because the FWA is generally not processed by human protections staff or IRB members, there may be incomplete follow-up to ensure completion of the suggested training. In recent years, the development of programs like the Collaborative Institutional Training Initiative ("CITI") and the University of Minnesota's training modules has made access to educational programs easier. However, some of this training is not as inclusive or interactive as it should be (for example, in the past the NIH training was suboptimal, did not provide comprehensive training, and may not have been focused on the role of the individual). Additionally, there are questions as to whether training programs are adequately revised as governing law and/or guidance changes. Consequently, it is very likely that the training recommended for key individuals by OHRP in the FWA has not been completed at many institutions.

(1b) What, if any, are the reasons for institutions not implementing OHRP's recommendations?

One of the key reasons why institutions may not initiate OHRP's recommended training is their lack of knowledge regarding the content of the FWA. Many institutions prepared the original FWA document years ago. Although they subsequently revise the FWA on a continuing basis (for example, to update Institutional Review Board ("IRB") membership), institutional personnel usually do not take note of any changes to the FWA and therefore are unaware of the educational suggestions made by OHRP. These recommendations are particularly likely to be overlooked given that they are buried within the FWA document. In addition, institutions may not implement the recommendations because they are simply suggested rather than required.

Instead, most institutions look to the governing regulations, OHRP guidance, and OHRP determination letters to determine what is required or considered to be best practices for training. As the issue of initial and continuing education is not clearly discussed in OHRP guidance, many institutions do not consider this a requirement.

Multiple other factors may cause an institution to fail to comply with OHRP's education recommendation. These factors include that an institution may not know how to implement such training or what the content of such training should be; an institution may fear that compliance will cause disruption with faculty or staff; an institution may lack the necessary funds or personnel to initiate training programs or massive educational sessions; or an institution may simply be complacent in complying with recommendations.

(1c) Has any failure of institutions to implement OHRP's recommendations been a significant contributing factor to noncompliance with the requirements of 45 CFR part 46 and inadequate protection of the rights and welfare of human subjects? If so, please provide examples.

OHRP's determination letters, as well as those issued by the Federal Drug Administration ("FDA"), are full of examples where a lack of education about regulations and guidance has led to noncompliance. The institutions whose FWAs were restricted by OHRP in 1999-2001 all shared a lack of understanding regarding the relevant regulations and guidance, across many levels of their organizations. More recent OHRP determination letters restricting or suspending FWAs also indicate, either directly or via the types of issues identified, that lack of education is key to the institutions' underlying problems. Typically, the person responsible for noncompliance did not know or did not understand the importance of a particular requirement or process. For example, unaware of the requirements, the Principal Investigator ("PI") or institution may not report an unanticipated problem involving risks to human subjects or others to the IRB, and the IRB may therefore be unable to report it to OHRP.

(1d) If failure of institutions to implement OHRP's recommendations has been a significant contributing factor to noncompliance with the requirements of 45 CFR part 46 and inadequate protection of the rights and welfare of human subjects, would promulgation of a regulation requiring institutions to implement training and education programs for certain individuals involved in the conduct, review or oversight of human subjects research be the best mechanism to address this problem, or should different mechanisms be used (for example, would it be better if OHRP instead issued additional guidance regarding training and education programs)?

DePaul believes that it would not be appropriate to issue a regulation that requires training and education, because regulations are generally too difficult to revise and update. For example, the current regulations have not been revised substantially since they were first issued in the 1980's, even though many sections have been identified as being unclear or even obsolete based upon the passage of time. A regulation would also impose a mandatory deadline which could be difficult to meet given that no additional funding would accompany the new requirements.

A clear and concise OHRP guidance document requiring training and education would be a far better mechanism to address potential noncompliance. In general, guidance documents may be revised much easier and faster than regulations. Moreover, even though they are not technically binding, most individuals in the IRB world (including AAHRPP) consider the OHRP guidance documents to be the ultimate authority on best practices in IRB policy and procedures. In other words, the industry essentially treats OHRP guidance documents as binding and would follow any training and education requirements appearing therein.

(1e) **Even if there are no data suggesting that failure of institutions to implement OHRP's recommendations regarding education and training has been a contributing factor in non-compliance with the requirements of 45 CFR part 46, are there other sound reasons for developing further guidance or a regulation regarding education and training, and if so, what are they?**

Although one cannot unequivocally say the majority of noncompliance issues occur due to lack of education, it is apparent from OHRP determination letters that adequate education and understanding is at the core of any noncompliance problems. If OHRP wants institutions to have programs on initial and continuing education for the research community, then it will need to state this fact explicitly. Although AAHRPP is steadily accrediting institutions, the process is slow and time-consuming, and may never reach institutions where the greatest risk to participants is present, because the institutions are too small to feel accreditation necessary or to justify the cost of the accreditation process. Only issuance of a guidance document from OHRP has the force and the ability to reach the majority of institutions where human subject research occurs.

(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)?**

DePaul recommends that all of the above receive some level of training. The persons with the greatest responsibility for the design and conduct of human subjects research should receive the greatest amount of training and education. Specifically, the most comprehensive and detailed training should be reserved for the investigators and their staff, the IRB Chairs, IRB members, and IRB staff. By contrast, the FWA signatory official and the Human Protections Administrator ("HPA") may not require the same level of detail regarding the regulations and their application, because this information may not be necessary for them to fulfill their role in the human protections program. Rather, these persons should understand the importance of the regulations, the FWA, and how all the key components work together to create an adequate Human Subjects Protection Program ("HSPP").

(3a) **Should further guidance or a regulation include provisions stipulating specific content for the training and education programs? 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))?**

Further guidance on training and education should identify specific content for training and education and should be as explicit as possible. Otherwise, there will be continued confusion about the nature and length of what is appropriate (for example, whether training should take a few minutes versus several hours to complete). Ideally, the guidance would categorize education and training according to (1) what is minimally required, and (2) what is optional but recommended. This would provide institutions with notice of what training and education threshold they must meet, while still permitting them the flexibility to adapt their programs to their individual research portfolio.

For example, DePaul recommends that the following items be identified by OHRP guidance as minimally required, versus optional but recommended, training and education:

Minimal Training/Education Requirements:

a) Historical background and foundations of research ethics, including a review of the Belmont Code, the Declaration of Helsinki, the Nuremberg Code, the Council for Organization of International and Medical Sciences ("CIOMS"), and the International Conference on Harmonization—Good Clinical Practices ("ICH-GCP");
b) Governing regulations and their key terminology, including those of the Department of Health and Human Services ("HHS") and the FDA;
c) Study design elements and how they relate to minimizing risk;
d) IRB and institutional considerations in the review process;
e) Basic IRB process for approval, levels of review, and specific institutional policies and processes related to the IRB review process;
f) Informed consent, including waiver of consent and waiver of documentation;
g) Privacy and confidentiality as applied to research;
h) Recruitment process and advertisements as applied to research; and
i) Required recordkeeping.

Optional Training/Education Recommendations:

a) State and local laws or regulations;
b) HIPAA;
c) IRB committee organization, responsibilities, and functions;
d) IRB office organization, responsibilities, and functions;

e) Institutional commitments under the FWA;
f) Reporting and monitoring;
g) Specific registry and biomedical protocols, such as emergency and treatment use;
h) Use of data, records, specimens, etc. from repositories; and
i) International research.

(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?

As previously noted, DePaul believes that training and education requirements should differ depending upon an individual's role in the human protection program and in the conduct of the research. Persons with the greatest responsibility for the design and conduct of human subjects research should be subject to the most stringent requirements. For example, as outlined above, it would not be necessary for an Institutional Official ("IO") or HPA to receive as detailed of a training session as a PI, IRB member, or IRB staff member. Additionally, not all persons conducting the actual research would require the same level of training—much of what might be necessary education for key research personnel would not be equally applicable to, for example, persons at a hired survey collection company.

(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?

There is a minimum level of knowledge that should be expected of all persons working with human subjects research. This minimum knowledge should include familiarity with the applicable regulations and guidance, information about the review process, review of the consent process and procedure, and an understanding of the documentation requirements, including the time period for which documents should be maintained. For a detailed list of suggestions, see the above response to question 3(a).

(3d) How often should the content of the materials used for this training be updated?

DePaul recommends that there be no specific schedule for updating training materials related to human subjects research. A specific timetable for training updates is simply too arbitrary, given the variance in institutional research protocols and practices. Rather, institutions should be encouraged to update training materials as needed, whenever regulations or guidance applicable to their research protocols are subject to significant change. In DePaul's experience, creating and implementing an institution-wide education program or policy is both time-consuming and expensive (as demonstrated by the implementation of HIPAA). Once staff have utilized resources to create and conduct education, it may be very difficult to go back and revise it in a timely manner when other pressing duties of the HSPP continually occupy personnel. At the most, OHRP guidance should specify that revisions can be made as necessary based upon revised or updated regulations or guidance.