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Assistant General Counsel

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<http://www.regulations.gov>  
Jeffrey Shuren, MD, JD  
Associate Commissioner  
U.S. FDA, Division of Dockets Management  
5630 Fishers Lane, Room 1061 (HFA – 305)  
Rockville, MD 20852

[humansubjectstraining@hhs.gov](mailto:humansubjectstraining@hhs.gov)  
Michael A. Carome, MD  
Captain, U.S. Public Health Service  
Office of Human Research Protection  
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**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these comments in response to the Food and Drug Administration's ("FDA") Notice of July 29, 2008 (regarding the *Draft Guidance for Sponsors, Clinical Investigators and Institutional Review Boards on Frequently Asked Questions – Statement of Investigator (Form FDA 1572)* and the Office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 OHRP 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.<sup>1</sup>

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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<sup>1</sup> 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.<sup>2</sup> 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,



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<sup>2</sup> See <https://www.trialstransformation.org/projects/priority-areas-for-ctti-projects/>

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