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Human Research Report

PROTECTING RESEARCHERS AND RESEARCH SUBJECTS

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New Guidance Includes Role Of Institutional Review Boards

The Food and Drug Administration (FDA) has issued a new draft guidance titled "Use of Electronic Informed Consent in Clinical Investigations: Questions and Answers."

> "The guidance provides recommendations for clinical investigators, sponsors, and institutional review boards (IRBs) on the use of electronic media and processes to obtain informed consent for FDA-regulated clinical investigations of medical products, including human drug and biological products, medical devices, and combinations thereof" (80 Fed. Reg. 12496-12497 at page 12496, March 9, emphasis added).

Before proceeding with our presentation of FDA's guidance, however, note that the federal Office for Human Research Protections (OHRP) has issued a joint announcement. That separate but related announcement seeks input to OHRP on whether or not the research community believes that the FDA guidance is sufficient or that OHRP ought to issue its own guidance on the same topic.

Should FDA's New Guidance Apply to Social and Behavioral Research Too?

> "Although the document [i.e., the guidance] is issued by FDA and is drafted as a guidance that would apply to FDA-regulated clinical investigations, OHRP is considering whether to adopt the positions and recommendations proposed in this guidance for research regulated under the HHS [Health and Human Services] protection of human subjects regulations, 45 CFR part 46, and to issue a joint OHRP and FDA guidance document on this topic when the final guidance document is developed. OHRP asks for public comment about whether a joint guidance document would be useful for the regulated community. In particular, OHRP is interested in public comment regarding whether FDA's draft guidance would be appropriate for all research regulated under 45 CFR part 46, including research studies other than clinical investigations or clinical trials, such as social and behavioral research studies.
>
> If different guidance should apply to social and behavioral research, or other non-FDA-regulated studies, OHRP asks that the public comments address how the guidance should differ from the proposed guidance for FDA-regulated clinical investigations.
>
> OHRP specifically welcomes feedback regarding when it might or might not be appropriate, for studies other than clinical trials, for OHRP to recommend that researchers verify that the person signing the informed consent form is the subject participating in the research.

NOTE #1: Quoted materials in this newsletter appear exactly as originally published in source documents, including any misspellings, grammatical errors, etc.

NOTE #2: Articles may be continued in subsequent issues.

Also In This Issue

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OHRP and FDA will consider these comments in deciding whether to issue a joint OHRP/FDA guidance document on this topic when the final guidance document is developed" (80 Fed. Reg. 12497-12498 at p. 12498, emphases added).

For persons wishing more information about the OHRP's announcement, contact: OHRP's Irene Stith-Coleman, Ph.D., at 240-453-6900, or send email to Irene.Stith-Coleman@hhs.gov.

For persons wishing to submit comments to OHRP, the fastest method is probably electronic by accessing the federal regulations Web site at http://www.regulations.gov, and submitting comments on Docket ID No. HHS-OPHS-2015-0002. Although the OHRP announcement does not have a comment deadline, the date of May 7 is listed in the "Dates" section. We can infer that May 7 is the OHRP comment deadline date, since May 8 is the FDA's comment deadline date.

Q&As Include IRB Responsibilities

The FDA's nine-page guidance is primarily composed of 14 Q&As about electronic informed consent documents, referred to as "eICs." The Q&As range from #1 ("How should the information in the eIC be presented to the subject?") to #14 ("What materials or documents will FDA require during an inspection?").

The responsibilities of IRBs are included, of course, as are a number of specific duties for researchers that can affect the IRBs' reviews, even if the term "IRB" does not appear in the title of the Q&A. For example, Q&A #7 addresses pediatric studies and includes the responsibility of IRBs without mentioning IRBs in the title of the Q&A.

Before we address the specifics of the Q&As, however, some basic information is warranted to understand what is meant by "eIC."

"For purposes of this guidance, *electronic informed consent* refers to using electronic systems and processes that may employ multiple electronic media (e.g., text, graphics, audio, video, podcasts and interactive Web sites, biological recognition devices, and card readers) to convey information related to the study and to obtain and document informed consent.

This guidance provides recommendations on procedures that may be followed when using an eIC to help:

- Ensure protection of the rights, safety, and welfare of human subjects
- Ensure the subject's comprehension of the information presented during the eIC process
- Ensure that appropriate documentation of consent is obtained when electronic media and processes are used to obtain informed consent[4] [FN #4: Investigators are required to prepare and maintain records as described in [21 CFR] §§312.62 and 812.140(a). Similarly, sponsors are required to maintain records relating to an investigation as described in §§312.57 and 812.140(b).]
- Ensure the quality and integrity of eIC data included in FDA applications and made available to FDA during inspections[5] [FN #5: For the purposes of this guidance, eIC data includes the template and site-specific versions of eIC, materials submitted to IRBs for review and approval, all amendments to the template and site-specific eICs, required informed consent elements presented to the subject during the eIC interview process, and the electronic signature of the subject, including the date when the subject or the subject's LAR [i.e., legally authorized representative] signed the eIC.]" (guidance, March, the underline emphasis is added; on the Web at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM436811.pdf).

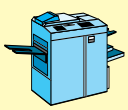
Specific IRB Roles Are Described

As noted above, Q&A #7 serves as an example containing a description of IRB duties. The context for Q&A #7 is research with children, as follows.

"**Q7. What special considerations should be given to the use of eIC for pediatric studies?**

[A] The eIC process can be used to obtain assent from pediatric subjects (when required) and parental permission from their parent(s) or guardian. The general requirements for informed consent, found in [21 CFR] §§50.25, 50.27, and 50.55, apply to parental permission.

Absent a waiver of the assent requirement, the IRB must determine that there are adequate provisions for soliciting the assent of children when, in the IRB's judgment, the children are capable of providing assent.[13] [FN #13: See 21 CFR 50.55(a).] In addition, the IRB must determine whether and how assent must be documented.[14] [FN #14: See 21 CFR 50.55(g).] The language and presentation of information must be understandable to the child, and the documentation of assent should be handled in the same way as documentation of informed consent/parental permission" (supra at page 6, emphases added). ©



Research Ethics, Subject Safety, and Emergencies

A new report from the Presidential Commission for the Study of Bioethical Issues (PCSBI) addresses key ethical and regulatory issues surrounding public health emergencies such as the Ebola virus. The 78-page report covers major issues regarding how the virus, and other public health emergencies, should be handled in the future.

Since our interests are with human subjects research, we shall focus on the report's "Part II: Health Planning and Response in Context," especially the section titled "Research Ethics During Public Health Emergencies." As usual, we shall present those portions that support recommendations, since it is those recommendations that can be used to support new legislation and/or regulations affecting researchers, Institutional Review Boards, and research institutions.

> "Public health emergencies can complicate ethical concerns common to the conduct of clinical research. The fear and desperation associated with epidemics, coupled with a heightened sense of urgency, raise challenges for the way in which ethical principles for human subjects research are interpreted and practically applied during a public health emergency" (report, February, p. 32, emphases added; on the Web at http://bioethics.gov/sites/default/files/Ethics-and-Ebola_PCSBI_508.pdf).

Research With Human Subjects in Epidemics

The best way to accurately assess experimental measures during an epidemic is to conduct testing during an actual epidemic, according to the PCSBI.

> "As a result, large clinical trials are currently planned or underway in Ebola-affected countries in western Africa to evaluate new Ebola vaccines and pharmacological treatments. These studies raise difficult ethical, scientific, and practical questions about how to best to design and conduct research during a public health emergency --particularly in a context characterized by poverty, vulnerability, and limited infrastructure. One question concerns whether conducting a randomized placebo-controlled trial to evaluate new preventive or therapeutic interventions for Ebola is ethically appropriate.
>
> In this section [of the report], the Bioethics Commission highlights two differing perspectives on this question: (1) that the priority for clinical research in the Ebola context should be to identify safe and effective interventions as efficiently and reliably as possible, and that randomized placebo-controlled trials are the best way to achieve this goal, and [versus] (2) that the priority for clinical research in the Ebola context should be to provide access to the potential benefits of experimental interventions to as many participants as possible using scientifically valid research designs.
>
> In its analysis, the Bioethics Commission underscores ethically relevant aspects of conducting clinical research in the current Ebola epidemic that might help address the tensions between these two perspectives while highlighting the importance of considering a range of trial designs -- recognizing that very different concerns arise during trials of *vaccines* involving healthy volunteers and *treatments* for research participants with an often fatal disease" (supra at p. 33, underline emphases added).

Is Placebo-Controlled the Only Way to Go?

First, the report describes the often favored placebo-controlled design argument.

> "Randomized placebo-controlled trials are considered the ideal scientific standard for determining the efficacy of a new treatment or vaccine. Researchers who support use of randomized placebo-controlled trial designs in Ebola research argue that these trials are the most efficient and powerful method for assessing the safety and effectiveness of available experimental interventions, both to protect participant and patient safety during the current Ebola epidemic ....
>
> In addition, they raise concerns about trial designs that do not involve a placebo arm, including their vulnerability to error such that credible results are unlikely and that, in the absence of credible results, it will be difficult to determine the safety, efficacy, and effectiveness of a new intervention.
>
> *Alternative trial designs might lead to invalid results*. Proponents of randomized placebo-controlled trials argue that the data generated by certain alternative trial designs might lack validity .... One proposed alternative to randomizing participants into treatment and control groups is to compare those taking an experimental intervention with historical control subjects. However, validity could be threatened if the historical control subjects differ in relevant ways from those in the clinical trial -- for example, if they are more ill or less ill, older or younger, are identified at a different stage of illness, received different kinds of medical care, are infected at a different stage of illness, received different kinds of medical care, are infected with a virus that might have mutated from past epidemics, or are different in unmeasured or unmeasurable ways" (supra at pp. 33-34). ©

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IRB-Approved Protocol Raises Questions on Risk Description

As we have been following, the controversy over "standards of care" research, and which risks must be explained to research subjects, continues unabated. The original impetus for the controversy is the now concluded SUPPORT study involving the use of different treatments (all of which were considered to fit in normal "standards of care" ranges) for dangerously premature infants. Although the Institutional Review Boards of the multisite study approved the informed consent form, that same consent (and, hence, the IRB reviews) have been severely criticized as unethical.

In past issues of HRR, we have presented portions of the draft guidance on this topic that was issued by the federal Office for Human Research Protections (OHRP) some time after conclusion of the SUPPORT study. The guidance is titled "Draft Guidance on Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care." Background information on the guidance appears in the FEDERAL REGISTER (79 Fed. Reg. 63629-63634, October 24, 2014).

This month we present another key portion of the guidance, since it is difficult to follow the opposing sides of the controversy over the guidance's recommendations without understanding what the guidance actually says. Specifically, we present here what the guidance says involving the intent of a relevant study, or what its "purpose" might be. The guidance uses a Q&A format. We have already presented Q&As #1 and #2.

"Purpose" of the Study and Risks for Subjects

[Q] "3. When is evaluating a risk in a research study considered to be a 'purpose' of the research study?

[A] The purposes of research are the aims or objectives that determine the design of the research study and provide the scientific and ethical justification for carrying it out. The evaluation of a risk is considered a purpose of the research when a research study is designed and conducted in order to ascertain the existence, extent or nature of a particular harm.

If a study is designed to discover the degree to which that particular harm will or will not occur, the possibility of that harm occurring is clearly foreseen by those responsible for the design and conduct of the study. The risks should accordingly be disclosed to the people who are being asked to be exposed to that risk as subjects of the study.

In the context of research evaluating standards of care, the evaluation of the risks in studies comparing standards of care that OHRP generally considers to be identified as 'purposes' of the research should be limited to evaluating those risks that are sufficiently important to justify the conduct of the study. The purposes of such studies should not be construed as necessarily including each and every one of the outcomes that may be measured as part of the study, but that are not part of the fundamental reasons for conducting the study.

Nor is the evaluation of any risk that is simply unknown or unrecognized to be considered a purpose of a research study. Only if the research study is deliberately designed to provide evidence about a particular identified risk is the evaluation of that risk to be considered a purpose of the research.

For example, if a research study is designed to include enough subjects to enable the analysis of the data to draw statistically significant conclusions about a particular risk, this would be a basis for considering the evaluation of that risk to be a purpose of the research" (guidance, emphases are added; on the Web at http://www.hhs.gov/ohrp/newsroom/rfc/comstdorcare.html).

A key aspect of the informed consent, which has been criticized by leading research ethics individuals and groups (but defended by others), is whether or not the risks in question were foreseeable ones.

Explaining "Reasonably Foreseeable Risks"

[Q] "4. Are the risks of research associated with the purposes of studies of standards of care 'reasonably foreseeable risks' that must be disclosed to prospective subjects in the informed consent process?

[A] The HHS regulations require that prospective subjects must be informed of the reasonably foreseeable risks of the research, so that they can take this into account in deciding whether or not to participate. Individuals being asked to consent to participate in such a research study may have preferences with respect to risks to which they might be willing to be exposed. The regulations include the following requirement for the disclosure of risks as part of the informed consent process:

(2) A description of any reasonably foreseeable risks or discomforts to the subject; (45 CFR 46 .116(a)(2))

If evaluating a particular risk of research associated with a standard of care is a purpose of the research, then in general OHRP considers that particular risk to be 'reasonably foreseeable.' Such reasonably foreseeable risks must be disclosed as risks in the informed consent process in accordance with ... 45 CFR 46.116(a)(2)." ©

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IRB Guidance Includes Method For Early Subject Enrollment

We return here to a topic we last covered in the October 2014 issue; namely, the contents of a guidance developed by the Food and Drug Administration for use by Institutional Review Boards and others. The guidance is titled "FDA Decisions for Investigational Device Exemption Clinical Investigations: Guidance for Sponsors, Clinical Investigators, Institutional Review Boards, and Food and Drug Administration Staff" (emphasis added to title).

The guidance describes various types of approvals that are available from FDA, and their respective requirements. For example, in the October 2014 HRR we presented the guidance's description of an "IDE Approval With Conditions." This month we present FDA's "Staged Approval" or "Staged Approval With Conditions."

IRBs should be familiar with this guidance since it can have a direct bearing on the appropriateness of a protocol's research plan, especially subject enrollment procedures and assessment of benefit-risk ratios. Before proceeding, note that FDA will accept comments on this guidance at any time.

Change in Enrollment May Prevent Disapproval

> "This guidance defines processes, termed 'staged approval' or 'staged approval with conditions' (both which are subsets of approval and approval with conditions decisions), by which FDA may grant IDE approval or approval with conditions for a portion of the intended study cohort, enabling certain outstanding questions to be answered concurrently with enrollment in this cohort. [FDA notes here that the term 'staged approval' is to be considered synonymous with both 'staged approval' and 'staged approval with conditions.']
>
> Staged approval permits the clinical investigation to begin in a timely manner while maintaining appropriate subject protections. In some cases, the sponsor proposes a staged enrollment in the IDE application. In other cases, the sponsor requests approval for the full subject cohort but, under certain circumstances described below, FDA may decide to grant staged approval for a limited number of subjects as an alternative to disapproving the IDE" (guidance, August 19, p. 8, emphasis added, http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM279107.pdf).

One of the advantages of this particular type of FDA approval is that it can permit a study to start sooner than it otherwise would.

> "As noted above, under staged clinical investigations, FDA will grant approval or approval with conditions for a portion of the planned subject cohort while the particular outstanding questions are addressed. FDA will grant approval with conditions if there are other issues that should be addressed within 45 days, which may include questions seeking clarification or information regarding the data that will be gathered to support future study expansion.
>
> Alternatively, if the FDA and the sponsor have agreed to the additional data that will be provided and no other outstanding issues remain to be addressed (i.e., under approval with condition(s)), a staged clinical investigation can receive approval, with enrollment limited to the number of subjects to be enrolled in the first stage" (supra at pp. 8-9, emphases added).

Benefit-Risk Ratio Is Key to Early Study Start

Accuracy of a protocol's assessment of benefit-risk ratios, and an IRB's review, may determine how soon a study can begin under such an approval.

> "If the benefit-risk profile based on the IDE submission is sufficiently favorable to justify enrollment of a portion of the study subjects, a staged clinical investigation may be appropriate to allow initiation of subject enrollment in a study while providing additional mitigation of risk by limiting exposure of the investigational device to a smaller subject population. Such an approach may be appropriate in the following situations:
>
> • Additional clinical confirmation of the safety profile is obtained by reviewing initial data from subjects enrolled early in the clinical investigation before enrolling the full subject cohort.
>
> • Additional non-clinical testing is needed to more fully characterize device performance to adequately evaluate the potential risks of the device, before permitting testing of the full subject cohort and is conducted concurrently with early enrollment in the clinical investigation.
>
> The sponsor will be permitted to expand enrollment once an IDE supplement containing the necessary additional information is submitted to FDA and found to be acceptable. In some cases, based on the information submitted, a partial expansion of enrollment may be granted (i.e., an additional stage of enrollment rather than expansion to full enrollment) while additional data are gathered to answer FDA's outstanding questions. In such cases, as with the first stage, the sponsor will be permitted to expand enrollment once a second IDE supplement ... is submitted to FDA ...." (supra, p. 9, emphasis added). ©

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IRBs, Regulatory Science, And Research With Minorities

Comments are due by April 27 on a topic that will impact certain funding priorities for the foreseeable future and, we believe, affect related protocols submitted for review by Institutional Review Boards. The area is one that has attracted more attention in the last few years; namely, the enrollment, retention, and participation of more members of subgroup populations as subjects in clinical trials.

> "The Food and Drug Administration ... is opening a docket to obtain information and comments on specific areas of public health concern for racial/ethnic demographic subgroup populations, focusing on certain disease areas where significant outcome differences maybe anticipated. The Agency is seeking public input on identifying areas that can be addressed through regulatory science research" (80 Fed. Reg. 10126-10127 at p. 10126, February 25, emphasis added).

The lead office for this activity is FDA's Office of Minority Health (OMH), as established in 2010 due to the Patient Protection and Affordable Care Act.

Procedures Designed to Reduce Racial Disparity

> "OMH advances FDA's regulatory mission in addressing the reduction of racial and ethnic health disparities and in achieving the highest standard of health for all. To achieve this mission, OMH has committed to identifying gaps in existing knowledge to shape further research projects intended to lead to better understanding of medical product clinical outcomes in racial/ethnic demographic subgroups ....
>
> We encourage comments to include supporting information regarding the topic addressed, such as previously published peer-reviewed literature or new research findings. These comments and information will support OMH in its development of a research agenda that will inform funding decisions for the next fiscal year .... In addition to input on improving clinical trial inclusion and outcome analysis, requested comments and information identifying disease areas with outcome differences for further study may include, but are not limited to, the following:
>
> • An area of study that could lead to a diagnostic or screening test based on the development and evaluation of biomarkers for a disease or condition that disproportionately impacts racial/ethnic demographic subgroups.
>
> • An area of study that could lead to changes in labeled indications, or dosages, for a single class of drug(s) or biologic(s) used to treat a disease or condition that disproportionately impacts racial/ethnic demographic subgroups.
>
> • An area of study that could lead to changes in the design or use of a device to treat a disease or condition that disproportionately impacts racial/ethnic demographic subgroups.
>
> • Research to identify effective ways to communicate with patients and consumers from racial/ethnic subgroups, including those with low health literacy and limited English proficiency, so they are informed about FDA actions (new approvals, warnings, recalls, etc.) that impact their health.
>
> • Research evaluating methods to accommodate cultural and language differences that can improve health communications to racial/ethnic subgroups, and assess the cost of these methods to the Government.
>
> • Research evaluating the impact of different formats and amounts of numerical information in FDA communications for patients, health care providers, health educators, and informal caregivers" (supra at p. 10127).

Encouraging Diversity of Human Subjects

Diversity in enrollment and participation of minority research subjects continues to be a prime goal of FDA.

> "A guiding principle for FDA in meeting the health needs of patients across the demographic spectrum is the importance of encouraging diversity in clinical trials. Thus, FDA is also interested in gaining input for improving clinical trials in therapeutic areas impacted by low rates of inclusion of racial/ethnic demographic subgroups populations, ranging from issues surrounding recruitment and participation in clinical trials to clinical outcome analysis of demographic subgroup populations ....
>
> Research in regulatory science is distinctive for developing new tools, standards, and approaches for assessing the safety, efficacy, quality, and performance of all FDA-regulated products. The results can help to transform the way medical products are developed, evaluated, and manufactured. Health disparities research with a regulatory focus seeks to expand and strengthen knowledge of, and the availability of data on, medical product clinical outcomes in racial/ethnic demographic subgroups, to inform healthcare decisions by providers and patients" (ibid, emphasis added).

For more information, contact: Christine Merenda, Office of Minority Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 2382, Silver Spring, MD 20993 at 301-796-8453, or fax to 301-847-8601, or send an e-mail to Christine.merenda@fda.hhs.gov. ©

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IRBs, Researchers, Subjects, And "Incidental Findings"

We return in this article to a topic we last addressed in the January HRR; namely, the regulatory and ethical responsibilities of researchers (and the Institutional Review Boards that review their protocols) regarding "incidental" and "secondary" research findings. As we discussed in the January issue (see page 6), the decision on whether or not to report such findings poses challenges for researchers and IRBs alike.

Accordingly, the topic of adequate informed consent in a clinical trial can become even more problematic.

> "In response to the trust imparted to them, researchers owe society and research participants obligations to design and implement research in a responsible manner. During the informed consent process, researchers should describe the types of incidental and secondary findings that might arise to ensure that participants are as informed as possible" ("Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts," Presidential Commission for the Study of Bioethical Issues, December, 2013, p. 86, emphasis added; on the Web at http://bioethics.gov/sites/default/files/FINALAnticipateCommunicate_PCSBI_0.pdf).

Informed Consent Even More Crucial

> "This includes, but is not limited to, disclosing anticipatable findings, any deliberately sought secondary findings, and the possibility of unanticipatable incidental findings.
>
> Researchers should also clearly communicate to participants the plan for disclosing and managing anticipatable incidental findings as well as any possible secondary findings, and the distinction between research and clinical care. This communication is essential to ensure that participants understand what to expect as a result of their decision to participate in research. Clarity with respect to whether and how researchers will disclose anticipatable and unanticipatable incidental findings, as well as any secondary findings that are deliberately sought, can help sustain public and participant trust in the research enterprise" (p. 87).

To complicate matters for researchers and IRBs, the timing of sharing information with research subjects also comes into play if much time has passed.

> "... researchers must consider whether disclosing incidental or secondary findings is still advisable given the potentially dated nature of the information ...." (supra at p. 79). ©

University's IRB Should Be Investigated, Says Group

The University of Minnesota's (UM's) human subject protection system and its Institutional Review Board (IRB) should be investigated, says the public health activist group known as Public Citizen. Public Citizen called on the federal Office for Human Research Protections (OHRP) to conduct such an investigation following release of the final report of an external evaluation of UM and revelations about its IRB operations and potential exposure of numerous human subjects to unnecessary risks.

> "In light of these findings, Public Citizen also calls on the Association for the Accreditation of Human Research Protection Programs (AAHRPP) to immediately rescind its accreditation of the human subjects protection program at UM.
>
> The report was commissioned by UM through a contract with AAHRPP and prepared by an external review team comprising six experts" ("In Wake of Report on University of Minnesota's Apparent Failure to Adequately Protect Human Research Subjects, Public Citizen Calls for Investigation," March 16, emphasis added; on the Web at http://www.citizen.org/pressroom/pressroomredirect.cfm?ID=5442).

IRB Had Insufficient Experts and Didn't Discuss Subject Risks/Benefits Enough

> " 'The alarming findings by the external review team echo some of the most serious instances of systemic failures of human subjects protections uncovered at major academic institutions over the past two decades,' said Dr. Michael Carome, director of Public Citizen's Health Research Group and formerly a senior official at OHRP. 'These findings also appear to represent a clear danger to the rights and welfare of human subjects enrolled in medical research studies at UM.' Among the findings, two things were most troubling.
>
> First, the UM medical institutional review board (IRB) appears to lack expertise among its members for the research that it reviews .... The external review team documented that from October 1, 2013, through September 30, 2014, more than 300 research protocols were reviewed from departments including adult hematology, oncology and transplant, cardiology, surgery and neurology. However, there were no individuals on the IRB during this time period with expertise in any of these medical disciplines" (ibid).

The second problem appeared to be failure of the IRB to adequately discuss subject risks and benefits. ©

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FDA Warning*

*See bottom of page 16 for HRR policy on investigation reporting

(Unless noted otherwise, recipients of a Warning Letter have 15 days to fix problems or explain how and when they will fix them. If not, they face sanctions with no additional warning and possible permanent disqualification from ever conducting research again with FDA-regulated products. This HRR feature includes Warning Letters sent to researchers, administrators, sponsors, and Institutional Review Boards.)

* * *

Warning Letter to: CEO,Wisconsin Hospital, (Part 1)
Investigation Period: Concluded on November 12, 2012
Warning Letter Date: March 25, 2013

* * *

Focus of Federal Investigation Is on Joint Institutional Review Board of Several Hospitals

"The purpose of this inspection was to determine whether the IRB's procedures for the protection of human subjects complied with Title 21 of the CODE OF FEDERAL REGULATIONS (CFR), parts 50 and 56. These regulations apply to institutions that, like ... [redacted by HRR] Healthcare, conduct clinical investigations of products regulated by FDA. This inspection revealed that ... [redacted by HRR] Healthcare's IRB has substantially failed to follow these regulations ....

At the conclusion of the inspection, Ms. ... [redacted by HRR] [of the FDA] presented the IRB Chairman, ... [redacted by HRR], with Form FDA 483, Inspectional Observations. We acknowledge receipt of the IRB's November 21, 2012, written response to the Form FDA 483. From our review of the FDA's establishment inspection report, the documents submitted with that report, and the IRB's written response, we conclude that the IRB did not adhere to the applicable statutory requirements and FDA regulations governing the protection of human subjects. We ... emphasize [that]:

1. The IRB failed to prepare, maintain, and follow required written procedures governing the functions and operations of the IRB (21 CFR 56.108(a), 21 CFR 56.108(b), and 21 CFR 56.115(a)(6)).

In order to fulfill the requirements of the IRB regulations, each IRB must prepare, maintain, and follow written procedures describing IRB functions and operations specified in the regulations.

... [Your] IRB provided two documents titled 'Policy and Procedure' concerning the IRB's activity to FDA. The first document is subtitled 'Institutional Review Board' and has an effective date of November, 2008. The second document is subtitled 'Clinical Trial Screening' and has an effective date of September 17, 2012. The IRB provided no other documents describing its procedures to FDA. These two documents do not contain all of the written procedures required under FDA's regulations. Specifically, your IRB failed to create or follow written procedures for:

- Conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution;
- Determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review;
- Ensuring prompt reporting to the IRB of any changes in research activity;
- Ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects; or ..." (emphases added).

IRB Fails to Report Its Review Decisions

"• Ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of:

- any unanticipated problems involving risks to human subjects or others;
- any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or
- any suspension or termination of IRB approval."

The multihospital health care system assured FDA that it would revise and update its Policy and Procedure manuals. FDA said that such an action would solve the problem, but the organization had to provide the new documents to prove its compliance.

The second of the organization's five areas of noncompliance involved review decisions of the IRB.

"2. The IRB failed to notify investigators and the institution in writing of its decision to approve or disapprove proposed research activities or of modifications required to secure IRB approval of the research activity (21 CFR 56 .109(e)) ....

Your IRB failed to provide written communication to investigators of its decisions to approve or disapprove research studies reviewed by the IRB." ©

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OHRP Determination*

*See bottom of page 16 for HRR policy on investigation reporting

Case: Undocumented Severe Adverse Reactions for Pediatric Research Participants (Part 8)
Investigating Agency: Office for Human Research Protections (OHRP) of the Department of Health and Human Services (HHS)
Case Included: A major medical center in New York State; inaccurate information in informed consent documents; and allegations involved 8-10 separate protocols
Case Concluded: January 7, 2008

Child Subject Has Severe Disease But That Did Not Violate Enrollment Criteria

We continue here with the investigated researcher's defense of his allergy studies with young children. In past HRR articles, we described how he defended his fairly extensive use of epinephrine (and that of his colleagues) to lessen the effects of allergic reactions in food challenge experiments.

Contradicting a whistleblower, he claimed that his use of the drug was not excessive. In addition, he quoted the informed consent form and the study's overall enrollment criteria to counter the whistleblower's claim that he had improperly enrolled some young children who did not fit the enrollment criteria.

For example, contrary to the whistleblower's claims, he pointed out that the enrollment exclusion criteria did not rule out patients who already had severe atopic dermatitis (eczema -- which the child had).

In combating another charge made against him, regarding exposure to beans for a child known to have an allergy to beans, he told his supervisor that:

> "Given that we have performed relatively few challenges to beans, we have reviewed the files of ... [redacted by OHRP] who have had such a challenge. Many of these have happened in the distant past. We believe we have identified the subject who is referred to in the allegation, who is one ... [redacted by OHRP] who participated in the ... [redacted by HRR] protocol. This subject underwent an oral food challenge to beans on .... [redacted by OHRP] is the only subject of the ... [redacted by OHRP] challenged to bean who had an open lesion on ... [redacted by OHRP]'s skin where .... [redacted by OHRP] was challenged, ... [redacted by OHRP] was challenged to white bean and kidney bean.
>
> As referred to in the OHRP letter, this child has very severe atopic dermatitis (eczema) and multiple food allergies .... [redacted by OHRP] was on an extremely limited diet due to ... [redacted by OHRP] food allergies and .... [redacted by OHRP] participation in this research protocol allowed us to identify foods that provoked allergic skin symptoms and those that could be added back into ... [redacted by OHRP] diet, and thus benefit his nutrition" (internal letter to the institution's Director of the Human Research Protection Program Office, January 4, 2007, p. 7 of 8, from the center's Chief of Pediatric Allergy & Immunology, emphasis added).

Subject's Nonreaction to Specific Allergen Meant He Could Participate in Experiment

"This child had persistent eczemalous changes including marked thickening and hyperpigmentation of his skin, extreme skin dryness, pruritus and scratching .... [redacted by OHRP] never experienced a severe anaphylactic reaction to white beans or kidney beans .... [redacted by OHRP] was admitted to the ... [redacted by HRR] ... [redacted by HRR] GCRC [General Clinical Research Center] on several occasions previously and was ... [redacted by OHRP] .... to our study physicians, research coordinators and GCRC nursing staff.

Prior to ... [redacted by OHRP]'s visit to the GCRC for bean challenge, the research nurse coordinators were in contact with ... [redacted by OHRP] to ensure that the child's skin symptoms were stable and that ... [redacted by OHRP] had infrequent scratching.

In the study physician's and research staffs' clinical judgment, ... [redacted by OHRP]'s skin condition on the day of the challenge was under relatively good control, which would allow accurate interpretation of any skin changes due to a food allergic reaction .... [redacted by OHRP]'s skin was generally dry and lichenified and ... [redacted by OHRP] also had open .... [redacted by OHRP] appeared relatively comfortable and was not scratching.

In addition, it was previously determined that the child had negative skin prick tests to the foods in question, i.e., no evidence of bean-specific IgE antibodies, indicating a <5% chance that these foods would precipitate an allergic reaction.

Given the importance of finding more foods for this child to eat, the lack of active flaring of ... [redacted by OHRP]'s skin over the vast majority of ... [redacted by OHRP]'s body, and the absence of IgE antibodies to the foods to be tested, it was decided that the benefit to the subject far outweighed the risk and the challenge was performed" (ibid). ©

Information about this newsletter is available on the Web at http://www.HumanSubjects.com

In Court

Case: Dolores Aderman v. The Trustees of the University of Pennsylvania, The Hospital of the University of Pennsylvania, James Wilson, M.D., Steven Raper, M.D., and Mark Batshaw, M.D. (Part 64)
Reference: No. 01-CV-6794
Court: United States District Court, E.D., Pennsylvania; Judge Anita Brody; Plaintiff's attorney Milstein, Defendant's attorney Gussack
Date: Case closed on March 24, 2003

Defense Says Research Subject Did Not "Contemporaneously" Witness Alleged Negligence

Last month we described how the defense claimed that neither Dr. Batshaw nor Dr. Raper had anything to do directly with obtaining the informed consent of the former subject, Aderman. In addition, said the defense, the various theories put forth by the plaintiff (e.g., negligence and battery) were not relevant for Dr. Batshaw either.

Note that Dr. Batshaw was represented separately from the university in court by Allan Starr, rather than by Nina Gussack who defended the university. Therefore, Gussack's arguments on behalf of the university do not appear at all at this point. After presenting his argument on the alleged nonrelevance of Batshaw, Starr then added the following.

"The only other comment I wanted to make, Your Honor, if I could for a moment --

THE COURT: Can we review the facts related to your client [i.e., Batshaw]?

MR. STARR: He is listed simply -- he is I guess the principal investigator on the protocol.

THE COURT: Okay.

MR. STARR: He did not participate in the obtaining of the consent, the discussion about what was going to happen.

He certainly did not participate in the injection or the hospitalization that led to those symptoms which the plaintiff claimed she received subsequent to the injection, but he clearly is a principal investigator.

I don't know of any theory articulated by plaintiff either in the complaint or under the law, that puts together those theories with Dr. Batshaw's role as an investigator.

THE COURT: All right.

MR. STARR: He may have other duties and responsibilities as an investigator. I'm not here to argue that he has no involvement, but as to the theories advanced by the plaintiff, I just don't see it.

Even -- I guess it was [claim] number 5 we were talking about before, I lost track which number, the negligence and infliction cases. Forget the bystander part of it [whereby a person suffers emotionally from being a bystander to an injurious event]. I don't care if -- she clearly isn't a bystander as to Jessie Gelsinger [who died about a year after Aderman participated in the experiment].

But accepting what plaintiff pleads and what he has argued as to Dr. Batshaw, we've got a situation where there's just, I guess I could say a neuron gap, A doesn't lead to B. What contemporaneous observation of a negligent event did Ms. Aderman perceive at the time she had anything to do with Dr. Batshaw? I think the clear answer is none --" (Transcript, May 18, 2002, pages 51-52, emphasis added).

Injury Claim Must Be Based On an Actual Observation

"THE COURT: Well --

MR. STARR: -- and contemporaneous observation of a perceived negligent event is, in fact, the cornerstone of the negligent infliction case. It's a case I actually argued in Pennsylvania Appellate Court *Solomen vs. Abington Hospital*. You've got to have that nexus. She just didn't have it. Now, it doesn't mean she may not have some theory out there for something, but she doesn't have a negligent infliction [of emotional distress] theory, certainly not as to Dr. Batshaw.

THE COURT: All right. Would you like to respond to that, Mr. Milstein?

MR. MILSTEIN: Sure. The answer is no. The answer is fairly simple, and again it goes to the unique quality and characteristic of what this human -- of this being a human experiment.

A subject in a human experiment is not the same as a donor who donates a kidney in a situation for his brother or his sister. A subject in a human experiment is governed by Federal Regulations.

There's a whole history attached to it dating back to the Nuremberg situation, through Tuskegee, through Willow Brook and all of that, and you have to understand the way human experiments are conducted in this country to understand how --

THE COURT: What --

MR. MILSTEIN: And let me answer the point about Dr. Batshaw.

He is -- he is a -- it's not simply he's just not the principal investigator. The way an experiment is conducted is, you had in this case three people, Dr. Batshaw, Dr. Raper and Dr. Wilson, and they sit together and they design a human experiment to test a hypothesis" (supra at pp. 52-54). ©

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In Congress

Multiple Institutional Review Board Assessments Listed Among Obstacles to Needed Research

A 42-page report (and at least as many pages of attachments) has been issued by Senators Lamar Alexander and Richard Burr, both Republicans. The R&D-oriented report is titled "Innovation for Healthier Americans: Identifying Opportunities for Meaningful Reform to Our Nation's Product Discovery and Development." The report is designed to serve as a rallying point for legislation designed to significantly expand and speed up biomedical research.

One of those initiatives is the identification and elimination of what the Senators consider to be unnecessary obstacles to more and better research.

> "The current approach to clinical trials leads to administrative inefficiencies, which in turn increase the time and costs associated with conducting clinical trials. Often, each entity involved in the clinical trial process, whether an academic research institution involved in an early Phase I trial or an innovator sponsoring a Phase III clinical trial, tends to conduct much if not all of this clinical trial work in a silo.
>
> As each entity involved in clinical trials employs its own approach to clinical trial processes and data collection, it results in an inconsistent and less coordinated approach to the trials and the data that emerge from them. In response, the medical product industry, government agencies, and nonprofit disease and patient groups have focused resources on improving the administration of clinical trials.
>
> Their efforts have looked to address key issues like requirements for multiple Institutional Review Board approvals for multiple trial sites, challenges in patient recruitment for clinical trials, and inefficient data collection and monitoring.
>
> Many initiatives and partnerships have arisen seeking to streamline clinical trials processes and foster innovative approaches to clinical trial design that more closely reflect medicine today and in the future. For example, through Transcelerate BioPharma, drug and device companies come together to streamline standards for data collection, site qualification, and investigator training.[61] [FN #61: http://www.transceleratebiopharmainc.com/our-initiatives/.] ....
>
> Additionally, NIH supports a plethora of clinical trial networks to increase patient engagement and involvement with clinical trials. Patient groups have themselves become more savvy and involved in clinical trials, becoming invaluable partners that accelerate patient identification and enrollment in clinical trials. Through these and other examples, we can see the promise of more efficient clinical trials, but the promise has not yet been realized. Currently, efforts are duplicated, best practices are not shared, and transformative innovations are not scaled up" (Senate report, January 29, emphases added; see http://www.help.senate.gov/imo/media/Innovation_for_Healthier_Americans.pdf).

Senate Predicts Future Research Legislation Targets

Given major obstacles like proliferating and cumbersome federal regulations, what can we expect Congress to do about it? HRR believes that most gamblers in recent years would have bet that Congress won't do much about it. Nevertheless, the report's "Conclusion" addresses relevant issues.

> "After 10 years and countless resources, programs, policies, and hard work, we still are not where we want to be to best serve American patients. Getting new medical products to patients is not a novel idea. Legislation, such as FDAMA in 1997 and FDASIA in 2012, emphasized the need for flexibility and provided the FDA with the tools to use that flexibility .... However, it still takes too long and costs too much for novel therapies that can be a patient's only hope to become available ....
>
> This Congress, the HELP [Health, Education, Labor & Pensions] Committee hopes to address five major themes to change the worrying trends and to get more medical products to the patients who need them:
>
> **1) It costs too much to bring medical products through the pipeline to patients.**
>
> **2) As science and technology advance, the discovery and development process takes too long for medical products to make their way to patients.**
>
> **3) FDA's responsibilities have grown to include many activities unrelated to the core function of regulating medical products to advance public health.**
>
> **4) The disparity in scientific knowledge at FDA and the fast pace of biomedical innovation are slowing, in some cases, stifling innovation in American medicine.**
>
> **5) A working FDA is essential to continuing biomedical innovation in the United States and maintaining America's global leadership in medical innovation"** (supra at p. 36, underline emphasis added). ©

In Agencies & Organizations

(Even if readers cannot respond to announcements by a stated official comment deadline, we recommend that interested readers still submit their comments anyway. Such comments can still make a difference. We have witnessed more than one instance where even a few comments have had significant effects on final regulations and policies.)

* * *

• **Environmental Protection Agency.** A meeting of the agency's ***Human Studies Review Board*** (or HSRB) was scheduled for April 22-23 in Arlington, Virginia. At this meeting, the HSRB will:

"... consider the ***ethical and scientific issues*** surrounding the following topics:

a. A Completed Study and Monograph Report for Backpack and Handgun Application of Liquid Spray in Utility Rights of Way (Agricultural Handlers Exposure Task Force).

b. A New Protocol for Field Testing of Skin Applied Mosquito Repellent Products (SC Johnson)" (80 Fed. Reg. 11986-11988 at p. 11988, March 5, emphasis added).

For more information, contact: Jim Downing at 202-564-2468 or send email to downing.jim@epa.gov.

• **Food and Drug Administration.** A ***Warning Letter*** was sent to Michele A. Sewell, M.D., of Stonecrest Pediatric and Adult Medicine in Lithonia, Georgia. Two inspectors from FDA reviewed the records of Sewell's research conducted on the investigational drug albiglutide, performed for GlaxoSmithKline.

The FDA investigation was conducted between June 17 and August 19 of 2013. Involved were two protocols, both of which were devoted to ***assessing the use of the drug in combating Type 2 diabetes***.

After reviewing Sewell's written response to FDA's Form FDA 483 ("Inspectional Observations"), and the research documents submitted with that form, FDA told her that:

"... we conclude that you did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations. We wish to emphasize the following:

1. You failed to ensure that the investigation was conducted according to the investigational plan (21 CFR 312.60) ....

2. You failed to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation (21 CFR 312.62(b)) .... [and]

3. You failed to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects (21 CFR 312.62 (a))" (July 6, 2014).

For more information, contact: Constance Cullity, M.D., M.P.H., Branch Chief, Good Clinical Practice Enforcement Branch, Food and Drug Administration, Bldg. 51, Rm. 5354, 10903 New Hampshire Ave., Silver Spring, MD 20993 at 301-796-3397, or fax to 301-847-8748.

• **Food and Drug Administration.** Comments are ***due by April 27*** on a new draft guidance titled "Medical Devices and Clinical Trial Design for the Treatment or Improvement in the Appearance of Fungally-Infected Nails." This guidance is relevant for the researchers and certain ***Institutional Review Boards that review relevant protocols.***

"This guidance is intended to provide recommendations when finalized regarding clinical trial design for medical devices intended either: (1) To provide improvement in the appearance of nails affected by onychomycosis, that is, to affect the structure/function of the nails or (2) to treat onychomycosis (fungal nail infection).

The FDA distinguishes these two conditions as target outcomes. The treatment of onychomycosis (an infectious disease) requires proof of stable elimination of the fungal organism, which is a medical endpoint. This outcome is distinct from outcomes limited to 'temporary increase in clear nail' in nails which are fungally infected, which is considered an aesthetic endpoint, and does not connote successful eradication of fungal infection.

The need for clinical performance data will be dependent on the design and use of the device. This guidance is intended to provide information related to both indications, when the device is applied to nails with confirmed fungal infection" (80 Fed. Reg. 4281-4282, January 27).

The guidance contains ***numerous instructions to researchers***. In turn, many of these instructions (e.g., on research design***, minimization of risks to certain subjects***, such as human subjects who have diabetes) are ***equally important for IRBs*** that review relevant research protocols.

For example, see Section IV ("Treatment of Onychomycosis"), in subsection A ("Regulatory considerations") on page 22 of the new guidance. The 31-page guidance is available on the Internet at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM431312.pdf).

For more information, contact: Neil Ogden, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg.

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66, Room G414, Silver Spring, MD 20993-0002 at 301-796-6397.

• **Food and Drug Administration.** Comments are ***due by May 4*** on a new draft guidance titled "Clinical Trial Imaging Endpoint Process Standards." This guidance is relevant for researchers and certain ***Institutional Review Boards*** that review protocols involving the use of imaging methods to assess an experiment's endpoint(s).

> "The purpose of this guidance is to assist sponsors in optimizing the quality of imaging data obtained in clinical trials intended to support approval of drugs and biological products. It focuses on imaging acquisition, display, archiving, and interpretation standards that FDA regards as important when imaging is used to assess the trial's primary endpoint or a component of that endpoint.
>
> The guidance describes the ***minimum standards a sponsor should use to help ensure that clinical trial imaging data are obtained in a manner that complies with a trial's protocol, maintains imaging data quality, and provides a verifiable record of the imaging process***" (80 Fed. Reg. 11998-11999 at page 11998, March 5, emphasis added).

This guidance is a revised version of one that FDA released previously on August 10, 2011. FDA received a number of comments on that earlier version, which ***led to a number of important changes to the guidance***. For example:

> "... (3) it is emphasized that imaging risks are best described in the clinical protocol and ***should be addressed in consent documents instead of including this information in the imaging charter*** [i.e., a description of the trial's imaging methods as contained in the protocol]" (ibid, emphasis added).

For more information, contact: Louis Marzella, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 5406, Silver Spring, MD 20993-0002 at 301-796-1414.

• **National Institutes of Health.** ***Effective May 1***, a new requirement will be in effect for all research projects funded by NIH's National Institute of Mental Health (NIMH).

> "Widespread data sharing by research communities adds significant value to research and accelerates the pace of discovery. The National Institute of Mental Health (NIMH) has established an informatics infrastructure to enable the sharing and use of data collected from ***human subjects in clinical research*** by the entire research community. ***Researchers funded by NIMH are strongly encouraged to deposit data from human subjects into this infrastructure***. In addition, non-NIMH funded researchers with related data are welcome to deposit their data ....
>
> ***As of May 1, 2015, NIMH expects investigators and their institutions to provide basic plans for following this Notice in the 'Data Sharing Plan'*** located in the Resource Sharing Plan section of grant applications. Compliance with this data sharing plan ***will become a special term and condition in the Notice of Award***" (NIH Notice No. NOT-MH-15-012, March 17, emphases are added; on the Web at http://grants.nih.gov/grants/guide/notice-files/NOT-MH-012.html).

For more information, contact: Gregory K. Farber, NIMH, at 301-435-0778, or via email to farberg@mail.nih.gov.

• **Office of Research Integrity.** A finding of research misconduct has been made in the case of Dong Xiao, Ph.D., a former Research Assistant Professor in the Department of Urology at the University of Pittsburg. His misconduct occurred in research funded by an NIH grant, and involved ***falsified data*** that appeared in a 2014 publication.

Xiao agreed to a three-year Voluntary Settlement Agreement that includes: (1) supervision of his research; (2) a certification by any employing institution that any research data of his can be authenticated; and (3) avoidance of any advising to any PHS entity.

For additional information, contact: Donald Wright, M.D., M.P.H., Acting Director, Office of Research Integrity, at 240-453-8200, or fax to 301-443-5351, or e-mail to AskORI@hhs.gov.

• **Secretary's Advisory Committee on Human Research Protections.** The latest meeting of the SACHRP was scheduled for March 24-25 in Rockville, Maryland. On March 24:

> "The Subpart A Subcommittee (SAS) ... [reviewing all the regular Subpart A regulations] will discuss ***draft recommendations on the use of newborn dried bloodspots in research*** ....
>
> The Subcommittee on Harmonization (SOH) ... will present recommendations on the ***research use of 'big data' and the intersection of the HHS and FDA regulations*** ....
>
> On March 25, the SOH will discuss the ***return of individual research results with special considerations regarding HIPAA and CLIA***; this will be followed by presentation of SOH ***recommendations on the FDA draft guidance 'General Considerations for Pediatric Studies for Drugs and Biologics'*** " (80 Fed. Reg. 10686, February 27, emphases added).

For more information, contact: Julia Gorey, J.D., Executive Director, Secretary's Advisory Committee on Human Research Protections, Dept. of Health and Human Services, at 240-453-8141, or fax to 240-453-6909, or send e-mail to Julia.Gorey@hhs.gov. ©

Compliance Conferences & Courses

By Kathleen J. Maloney, M.Ed., Associate Editor

• **April 15, 2015**, in Philadelphia, Pennsylvania: **"IRB (Institutional Review Board) 201."** This Regional Program is presented by Public Responsibility in Medicine & Research (PRIM&R), with the meetings to be held at the Sonesta Philadelphia Downtown at 215-561-7500. The topics will include: an overview of research ethics and regulations; criteria for IRB approval of research; minimizing risks to participants; equitable human subject selection; documentation of informed consent; monitoring subject safety; privacy and confidentiality; undue influence or coercion of subjects; and IRB members and conflicts of interest. Contact: PRIM&R, Suite 720, 20 Park Plaza, Boston, MA 02216 at 617-423-4112, or fax to 617-423-1185, or e-mail to info@primr.org, or see their Web site at www.primr.org.

• **April 16-17, 2015**, in Philadelphia, Pennsylvania: **"IRB (Institutional Review Board) Administrator 201."** This program is presented by Public Responsibility in Medicine & Research (PRIM&R). The meetings will be held at the Sonesta Philadelphia Downtown at 215-561-7500. The topics will include: the relationships between IRBs or RECs (Research Ethics Committees), their institutions, and institutions' researchers; establishing effective communications between the involved parties; determining which projects require compliance reviews; when informed consent or documentation may be waived; what questions to pose to researchers; and determining the important elements of IRB/REC Reliance Agreements. Contact: PRIM&R, Ste. 720, 20 Park Plaza, Boston, MA 02216 at 617-423-4112, or fax to 617-423-1185, or e-mail to info@primr.org, or see their Web site at www.primr.org.

• **April 16-17, 2015**, in San Francisco, California: **"Protecting Human Research Participants -- Legal, Ethical, and Practical Considerations."** This course will be presented by the Society of Clinical Research Associates (SoCRA), with meetings to be held at the Holiday Inn Golden Gateway. Topics include: methods used to identify and manage investigator and IRB members' conflicts of interest; ethical considerations in pediatric research; the role of study coordinators in protecting research subjects; legal issues in clinical research; the importance of continuing education for IRB members; and training in human subjects protections for clinical trial professionals. Contact: Conference Registrar, SoCRA, 530 West Butler Avenue, Chalfont, PA 18914 at 800-762-7292, or fax to 215-822-8633, or send e-mail to Office@SoCRA.org.

• **May 5, 2015**, Webinar (10:00 a.m. - 11:30 a.m. ET): **"Single IRB Review for Multisite Studies: Promoting Quality Review and Oversight."** This Webinar (free for AAHRPP clients) is presented by AAHRPP. This Webinar will discuss the SACHRP recommendations on single IRB review; the consideration of local context and standards; participant safety and postapproval monitoring; the contents of Authorization Agreements; and what information must be gathered and maintained by the single IRB of record in such situations. Contact: Sandra Jackson or Ivan Billings by email to webinar@aahrpp.org.

• **May 7, 2015**, Webinar (3:30 p.m. - 5:00 p.m. ET): **"Single IRB Review for Multisite Studies: Promoting Quality Review and Oversight."** This Webinar (free for AAHRPP clients) is presented by the AAHRPP. This Webinar will discuss the SACHRP recommendations on single IRB review; the consideration of local context and standards; participant safety and postapproval monitoring; the contents of Authorization Agreements; and what information must be gathered and maintained by the single IRB of record in such situations. Contact: Sandra Jackson or Ivan Billings by email to webinar@aahrpp.org.

• **May 7-8, 2015**, in San Diego, California: **"9th Annual Device Research & Regulatory Conference."** This conference is presented by the Society of Clinical Research Associates (SoCRA), with the meetings to be held at the Sheraton San Diego at 619-291-2900. The topics include: the 510(k) submission process; using human factors engineering to reduce medical errors; physiological research; U.S. versus EU research regulations; the role of IRBs in reviewing device research; FDA inspections of IRBs; and developing an IDE. Contact: Conference Registrar, SoCRA, 530 W. Butler Avenue, Chalfont, PA 18914 at 800-762-7292, or fax to 215-822-8633, or send e-mail to Office@SoCRA.org, or see their Web site at www.SoCRA.org.

• **May 13-14, 2015**, in Cincinnati, Ohio: **"FDA Clinical Trial Requirements, Regulations, Compliance, and GCP."** This conference will be presented by the Society of Clinical Research Associates (SoCRA) and FDA. The topics will include: informed consent; how FDA performs inspections of clinical investigators; the ethics of clinical research related to patient treatment; medical and regulatory components of adverse event reporting; fraud in clinical research; the duties and responsibilities of Institutional Review Boards (IRBs); informed consent requirements; what the FDA expects of clinical trials; and sanctions used by the

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FDA against institutional and IRB noncompliance. Contact: Conference Registrar, SoCRA, 530 West Butler Avenue, Chalfont, PA 18914 at 800-762-7292, or fax to 215-822-8633, or send e-mail to Office@SoCRA.org, or see their Web site at www.SoCRA.org.

• **May 17-20, 2015**, in Arlington, Virginia: **"MAGI's Clinical Research Conference - 2015 East."** This conference will be presented by MAGI (Model Agreements & Guidelines International), and cosponsored by many groups. Meetings will be held at The Renaissance Capital View Hotel. The 90+ workshops and sessions over multiple topic tracks will include: recent developments in human subjects protection regulations; FDA vs. OHRP vs. ICH requirements; adverse event reporting; human subject recruitment; subject injury and indemnification; weighing risks vs. benefits for human subjects; and IRB best practices. Contact: Norman Goldfarb, Chairman, MAGI, 2249 1/2 Sutter Street, San Francisco, CA 94115 at 650-465-0119, or fax to 855-734-2366, or send an e-mail to ngoldfarb@magiworld.org.

• **May 19-21, 2015**, in Chicago, Illinois: The **"2015 AAHRPP Conference."** This conference will be presented by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP), with the meetings to be held at the Chicago Hilton, 720 South Michigan Avenue at 866-460-7456. The topics will include: an overview of the AAHRPP accreditation process; human research protections in global research; biobanking and large data sets; IRB considerations in social media research; the challenges of IRB reviews of comparative effectiveness studies; and working with central IRBs. Contact: Conference Registrar, AAHRPP, 2301 M Street, N.W., Suite 500, Washington, D.C. 20037 at 202-783-1112, or send a fax to 202-783-1113, or send an e-mail to accredit@aahrpp.org, or see their Internet Web site at www.aahrpp.org.

• **May 23, 2015,** in Freeport, Maine: **"2015: 7th Annual Research Integrity Symposium."** This symposium will be offered by the University of Southern Maine's Office of Research Integrity and Outreach, with meetings to be held at the Hilton Garden Inn at 297-865-1433. The topics will include: preventing and responding to data security incidents; graduate student research misconduct; and unique requirements for human research protections in the DoD and VA. Contact: Tina Aubut at 207-780-4517.

• **June 2-5, 2015**, in Washington, D.C.: **"Intensive Bioethics Course 41."** This course will be presented by the Kennedy Institute of Ethics at Georgetown University. The topics will include: beneficence and non-maleficence; distinctions between research and practice; genomics; research ethics; and big pharma. Contact: Course Coordinator, Kennedy Institute of Ethics, Georgetown University, Box 571212, Washington, D.C. 20057-1212 at 202-687-8099, or fax to 202-687-8089, or see their Web site at http://kennedyinstitute.georgetown.edu.

• **June 22-25, 2015**, in Boston, Massachusetts: **"Ethical Issues in Global Health Research."** This course is sponsored by the Harvard School of Public Health and Public Responsibility in Medicine & Research (or PRIM&R). The meetings will be held at the Harvard T.H. Chan School of Public Health, FXB Building, 651 Huntington Ave., Boston, MA 02115 at 617-432-2100. Lodging is available at The Brookline Courtyard Marriott at 617-734-1393. The topics will include: guiding principles for clinical trials data sharing; IRB responsibilities in global research; the use of deception in research; human subjects research compliance, ethics, and logistics in global research; challenges and recommendations in conducting public health studies; providing equivalent protections when reviewing international research; conflict of interest in global research; increasing IRB review efficiency; issues in genetic research; study monitoring and regulatory compliance in global research; and mock IRB reviews. Contact: Program on Ethical Issues in International Health Research, Harvard School of Public Health, 665 Huntington Avenue, Building 1-1210, Boston, MA 02115 at 617-432-2100; or Conference Coordinator at PRIM&R at info@primr.org.

• **July 9-10, 2015,** in San Francisco, California: **"Harnessing Social Media to Advance Clinical Research."** This conference is presented by the Society of Clinical Research Associates (SoCRA), with the meetings to be held at the Holiday Inn Golden Gateway at 415-441-4000. Topics include: social media and IRBs; ethical debates over the Facebook Experiment; challenges in applying federal regulations to clinical trials involving social media; and human subject recruitment and retention using social media. Contact: Conference Registrar, SoCRA, 530 West Butler Avenue, Chalfont, PA 18914 at 800-762-7292, or send e-mail to Office@SoCRA.org. ©

Please remember to say you saw it in the HUMAN RESEARCH REPORT

If you will host a conference on research compliance issues, please send us the details. **There is no charge for such a listing.** Preference on listings is given to HRR subscribers, and first priority goes to human research protection listings. Accuracy of information depends on the sources used and the details are subject to change without notice. Readers should contact conference registrars directly to verify information. **Our receipt deadline for publication of a listing is the 1st of the month,** to be printed in HRR in the ***following*** month. Please send your listing to Kathleen@HumanSubjects.com.

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Dennis M. Maloney, Ph.D., is the founding editor and publisher of the HUMAN RESEARCH REPORT. Dr. Maloney monitors a number of professional disciplines to keep readers up-to-date on human experimentation topics and events. As the author, coauthor, or editor of over 200 publications, he has written extensively for professional audiences and for the public. His acclaimed book on human research participants, *Protection of Human Research Subjects: A Practical Guide to Federal Laws and Regulations*, was published in 1984 by Plenum Press in New York.

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Experienced in supervising both basic and applied research studies, he has faced the difficulties of constructing complete yet understandable informed consent documents and research protocols for the approval of Institutional Review Boards (IRBs). He has developed a wide range of successful grant proposals (over $20,000,000 in awards) for funding from local, state, and federal government agencies, corporations, private and corporate foundations, and individual philanthropists.

As the founding member of an IRB, and later serving as its chairman, Dr. Maloney is familiar with the responsibilities and the challenges undertaken by IRBs which strive to protect human research subjects while still encouraging important research. He has assisted in drafting human service legislation and has analyzed lawsuits in a series of workshop lectures. A member of many professional organizations, he has also served as the chairman of a national committee on legal issues and human services. The Deem Corporation is a registered member of the Better Business Bureau, the BBB Honor Roll, and the Internet-based BBB OnLine Reliability Program. Contents of this newsletter are by Dr. Maloney unless indicated otherwise.

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