Memorandum

To: All Investigators and staff potentially involved in the conduct or oversight of Human Research/Clinical Investigation

From: Rosalie K. Crouch, Ph.D.
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Re: Clarification of Educational Requirements for Conducting Human Research

Date: October 4, 2001

1. This memorandum is being issued jointly by the Provost's Office at MUSC and the Research Service at the Ralph H. Johnson VA Medical Center. It is intended to clarify our policy for educational requirements for conducting or overseeing human research by MUSC and VA faculty, administration, and staff.

   This memorandum is lengthy. It is being distributed in response to a flurry of feedback and questions from our valued faculty and staff, many of whom have expressed concern, dismay, anger and even outrage at what is perceived to be an unnecessary infringement on their time and energies. Thus, we feel that a detailed explanation of the national and local policies regarding the topic of educational requirements for conducting human research may be helpful. It is also apparent that we need to clarify precisely who must complete these requirements. We will address both issues in this memorandum. For those of you who wish to skip the explanations, you may proceed to sections #7-#12.

2. **Rationale**: The ethical conduct of research on human subjects is an essential component our research mission. The principles of the ethical conduct of research are delineated in the following documents:

   a. the Declaration of Helsinki (http://ohsr.od.nih.gov/helsinki.php3),
   b. the Nuremberg Code (http://ohsr.od.nih.gov/nuremberg.php3),
   c. the Belmont Report (http://ohsr.od.nih.gov/mpa/belmont.php3)
   d. the Code of Federal Regulations-PHS (45 CFR Part 46- http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm)
   e. the Code of Federal Regulations-FDA (21 CFR Parts 50 and 56- (http://www.fda.gov/cdrh/manual/appendb.html)
   f. VA handbook 1200.5 (http://www.va.gov/resdev/directive/Human.doc)

   As recipients of federal funding, our institutions are required to ensure that individuals performing or overseeing research on human subjects are educated on the ethical conduct of research. Specific guidelines have been issued by the Office for Human Research Protection OHRP- formerly called Office for Protection from Research Risks) in the United States Public Health Service regarding the responsibilities of individuals and institutions for compliance with the ethical conduct of research. For specific guidance on the educational requirements, please refer to (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-061.html) and (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html).
   Those two notices are also provided to you as attachments #1 and #2 to this memorandum.

   The VA has separate and more specific requirements as outlined in a policy memorandum from Dr. John Feussner (VA Chief Research Officer) dated March 14, 2001 (on file in VA R&D Office).

3. **Background**: A number of high profile research programs have been suspended for issues dealing with non-compliance with federal policies and/or good practices. These include some of the most highly respected academic medical centers in our country, such as the University of Pennsylvania, Duke University, the West Los Angeles VA Health System, and most recently Johns Hopkins University. Many other institutions have received "Compliance Activities: Letters of Determination" from OHRP within the last two years (http://ohrp.osophs.dhhs.gov/detrm_letrs/lindex.htm). A perusal of these letters is very sobering. Our Congress and the lay press have taken a keen interest in these happenings, and have weighed in with scathing editorials, exposes and Congressional inquiries. Thus, the public and our government demand both individual and institutional accountability.

   As a result, numerous agencies have been charged with oversight duties regarding research risks protection. These include OHRP, FDA, and the VA through a new office called ORCA (Office for Research Compliance and Assurance), as well as a virtual alphabet soup of others. Our Institutional Review Board (IRB) now needs to be certified by both VA and AAMC chartered organizations. Our IRB and the VA Research and Development Service will be site-visited in early 2002 by the National Committee for Quality Assurance- NCQA (http://www.ncqa.org/). They have provided us with a 90 page checklist for the upcoming

site-visit. Many of the audit points deal directly and indirectly with institutional and individual efforts to create and maintain a 'culture of compliance' and to embrace an educational program dealing with research compliance for staff and faculty.

Scrupulous external oversight of our efforts to develop excellence and rigorous compliance in the ethical conduct of research is now a reality. If we are not prepared to strive for excellence in this endeavor, we are likely to pay a high price in terms of time and dollars lost, and in terms of reputation and prestige. Despite this reality, many institutions continue to make the same costly mistakes. These mistakes are clearly documented in the public record by OHRP under "common findings" at http://ohrp.osophs.dhhs.gov/info.htm.

Our institutions can address many of the common findings, and we are doing so. Others require the full cooperation and assistance of our faculty. If we don't all pull together, we may suffer the same fate as has befallen research giants such as Johns Hopkins University and Duke University. Johns Hopkins University and many of its faculty refused to accept the gravity of this issue when they assumed a combative posture during an OHRP inquiry. The humiliating consequences of the subsequent shutdown of their research program is the subject a Baltimore Sun piece published on September 27, 2001 (http://www.sunspot.net/news/health/bal-te.md.hopkins27sep27.story?coll=bal%2Dhome%2Dheadlines).

4. **Approach to the Issue**: We must develop an educational program for conducting human research here. Ideally, this program would be the same at MUSC and at the Ralph H Johnson VA Medical Center. It makes no sense to duplicate these programs. The National VA Research Service has mandated certain elements required for this required program for all local VA Research Services. This mandate requires that investigators and personnel involved in research on human subjects or tissues take some form of tutorial that has a post-test component. Moreover, there are numerous required elements that must be met for the educational program to be acceptable. **The NIH module** (http://cme.nci.nih.gov/ or http://ohsr.od.nih.gov/) **that many of us completed last year as a stopgap measure is no longer acceptable to the VA**. It does not have a post-test and does not adequately cover VA and FDA regulations.

   We have every reason to believe that the NIH module is inadequate and will soon be deemed unacceptable by auditing and accreditation bodies. This impression is based upon (1) information gathered by several of our faculty and staff who have participated in OHRP and VA site visits, (2) by our own local experiences in being site visited by federal regulators, (3) and by personal communications with highly placed OHRP staff. Indeed, (4) our own internal audits have revealed the need for more detailed training than is provided by the NIH module.

   Thus, we were faced with the following question: Where might one turn to meet the stringent guidelines without subjecting our investigators to excessive inconvenience? We wish to document that we have performed a thorough examination of many options available to us. We have examined several different programs that have a post-test requirement and which contain the elements of content deemed essential by the VA. We used the AAMC web site (http://www.aamc.org/research/dbr/compliance/curricula.htm) as a starting point. After examination of a number of options, we established that the University of Miami course fulfills those requirements (http://www.miami.edu/citireg for registration; http://www.ci4.miami.edu/courses/irbtraining for the course).

   The Miami course was developed by a consortium of universities to meet the spirit and letter of the **law** as outlined in the Code of Federal Regulations and of **federal policy** as outlined in VA handbook 1200.5 (http://www.va.gov/resdev/directive/Human.doc) and in attachments 1 and 2.

   Some of you believe that this course is too comprehensive. This is a potentially fruitful area for discussion that falls under the "spirit" of the law category because we have established this policy locally. **However, we would like to emphasize that the Miami University Internet course is now the standard that is required at 82 different institutions.** We admit that there are, in fact, several Internet courses that are not as comprehensive as the Miami University course. However, they do not meet the requirements of the VA either in content or by lack of a post-test. Three examples that do not meet the VA requirements are provided below:

   University of Minnesota (http://www.research.umn.edu/consent/),
   University of Michigan (http://www.umich.edu/~drda/index.html),
   UCSF (http://www.ucsf.edu/ora/chr/chr_training.htm#trainA)

   Our policy is completely in line with those of other institutions known for their excellent IRB and research education programs, such as those from:

   University of Kentucky (http://www.rgs.uky.edu/ori/humantrain.html),
   University of Rochester (http://www.urmc.rochester.edu/rsrb/),
   UCLA (http://training.arc.ucla.edu/),
   Indiana University (http://www.iupui.edu/~resgrad/Human%20Subjects/StartPage.html),
   Duke University (http://irb.mc.duke.edu/certification.htm),
   Columbia University (http://cpmcnet.columbia.edu/research/gcp.htm)

We would also like to point out that the University of Rochester course (which is a rigorous book-based program) is now the second most commonly required course.

5. **Who should take the Miami Internet course?**

Definitions from 45 CFR Part 46
(http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm#46.102)

In order to help you assess whether one must participate in the required educational activity, we have provided some definitions from the Code of Federal Regulations.

"***Research*** means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities."

MUSC/VA comment: In practical terms, if you plan to publish the work, present it at a scientific meeting, or otherwise intend to use it for scholarly purpose, it is probably research. If you are not sure, please consult one of our IRB's.

"***Human subject*** means a living individual about whom an investigator (whether professional or student) conducting research obtains:
(1) data through intervention or interaction with the individual, or
(2) identifiable private information."

MUSC/VA comment: This means that use of tissues from living patients or examination of their medical records for the purpose of research qualifies as research on a human subject. If you are not sure, please consult one of our IRB's.

6. **Points for consideration from** http://grants.nih.gov/grants/policy/hs_educ_faq.htm.

"You may be performing human subjects research that qualifies for "exempt status" as determined by the IRB. Please note that exempt status does not mean exempt from IRB review. However, that research is not necessarily exempt from the educational requirements."

MUSC/VA comment: Research using human tissues (including autopsy or banked specimens) almost always will require completion of the course.
Tissue collection is governed by SC State Law-the IRB has requested that all use of human tissue in research be submitted to the IRB for review.

7. **WE HAVE EXTENDED THE DEADLINE FOR COMPLETING THE HUMAN RESEARCH EDUCATION REQUIREMENT TO DECEMBER 3, 2001.**

Because many of you have raised questions about who is required to complete the Miami University Internet course, we have agreed to extend the deadline by one month, to December 3, 2001.

8. **The nitty-gritty…who must complete the educational course by December 3, 2001?**

a. If you do not perform or oversee the conduct of human subjects research, you are not required to take the course. Some examples of people who do not have to complete this course would be secretaries or investigators who perform work solely on animals and non-human cells. *The exception to this guideline is that members of the VA IACUC, VA Biosafety Committee, and VA R&D Service office staff are required to complete the course.*

b. Investigators participating in human subjects research must complete the course. Investigators include PI's, collaborators, consultants, students, post-doctoral fellows, research assistants, research nurses, and technicians directly involved in the conduct of human subjects research. *In some cases it may be difficult to determine whether an individual qualifies as an investigator*. If one is going to author an abstract, manuscript, or presentation, or if one is obtaining informed consent from human research subjects, it is our view that they are investigators and should complete the course. *If you are not certain, please consult with Dr. Conradi or Dr. Raymond.*

c. IRB members and VA R&D Committee members must complete the course regardless of whether they perform human subjects research in their own investigative programs.

d. Individuals with institutional signatory or oversight authority for research at MUSC and the Ralph H. Johnson VA Medical Centers (e.g. the administrators) must complete the course. These include the Medical Center Director and Chief of Staff at the VA, the President and Provost of MUSC, Deans, Assistant/Associate Deans, Department Chairs, and Divisional Directors.

e. Research compliance officers and research audit team members must complete the course.

9. **Will we consider options other than the Miami University Internet Course?**

Please note that we are willing to accommodate reasonable substitutions for the University of Miami Internet Course. Some of the Internet courses listed on the bottom of page 2 might be reasonable substitutes for the University of Miami course. **As noted earlier in this memorandum, the NIH Internet module is not an acceptable substitute**. If you have recently completed a course with substantially similar content to the University of Miami course (with scored post-test) and would like for that to substitute for the University of Miami course, please send to Dr. Conradi and/or Dr. Raymond a cover letter, certificate of completion and a web-link or syllabus so that we can determine whether it meets guidelines. Feel free to pre-consult one of them prior to taking an alternate course (this is recommended).

Please also be aware that completion of the course does not fulfill requirements for continuing education in human subjects research. We are currently considering various mechanisms for all of us to fulfill future requirements for continuing education, and we will be seeking faculty input regarding various options.

10. **Avenue for Feedback**

Constructive criticism, comments and expressions of concern will be welcomed. We respectfully request that they be conveyed with professionalism.

The appropriate avenue for receipt of comments (other than the clarifications described in #8) is through Dr. John Raymond (2-1106; raymondjmusc.edu; beeper 14669) or through Dr. Ed Conradi (2-4148; conradie@musc.edu) until November 1, 2001.

After November 1, 2001, we request that you observe the "chain of command" and route your comments through your Department Chair and/or Divisional Director.

11. If you believe you have received this memorandum in error, please forgive us for inconveniencing you. We hope to construct mailing lists targeted specifically to human subjects investigators in the near future. This will be facilitated by the orderly completion of the human subjects training by those to whom it applies. Thank you.

12. EXECUTIVE SUMMARY

a. The deadline for completing the Miami University Internet course has been extended until December 3, 2001.
b. If you do not perform research on human subjects, data or tissues, you do not need to take the course (please see points #5, 6, and 8). This policy applies at both VA and MUSC.
c. If you perform research on human subjects, data or tissues, you need to take the course. If you supervise or oversee such research, you need to take the course. We have further clarified who should take the course (see point #8). The definitions for 'human subjects' and 'research' from the Code of Federal Regulations are provided in point #5.
d. We will consider alternate training exercises, so long as they have substantially similar content to the University of Miami course (with scored post-test). Pre-consultation with Drs. Raymond and/or Conradi is STRONGLY advised (see point #4).
e. The appropriate avenue for feedback has been delineated (see point #10)

Note: Initialed copies of this memorandum are available in the VA R&D Office and the Provost's office at MUSC.

There are two attachments to this memorandum.

Attachment #1

REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS

Release Date: June 5, 2000 (Revised August 25, 2000)

NOTICE: OD-00-039

National Institutes of Health

Policy: Beginning on October 1, 2000, the NIH will require education on the protection of human research participants for all investigators submitting NIH applications for grants or proposals for contracts or receiving new or non-competing awards for research involving human subjects.

Background: To bolster the Federal commitment to the protection of human research participants, several new initiatives to strengthen government oversight of medical research were announced by HHS Secretary Shalala on May 30, 2000. This announcement also reminds institutions of their responsibility to oversee their clinical investigators and institutional review boards (IRBs). One of the new initiatives addresses education and training. This NIH announcement is developed in response to the Secretary's directive.

Implementation: Before funds are awarded for competing applications or contract proposals involving human subjects, investigators must provide a description of education completed in the protection of human subjects for each individual identified as "key personnel" in the proposed research. Key personnel include all individuals responsible for the design and conduct of the study. The description of education will be submitted in a cover letter that accompanies the description of Other Support, IRB approval, and other information in accordance with Just-in-Time procedures. The use of a cover letter is also acceptable for contract proposals. After October 1, 2000, investigators submitting non-competing renewal applications for grants or annual reports for research and development contracts that involves human subjects research must also include a description of such education in their annual progress reports. This NIH policy will eventually be superceded by the DHHS Office of Research Integrity's institutional assurance on the responsible conduct of research, which is described below.

Related Training Requirement: The Office of Research Integrity (ORI), Department of Health and Human Services, is developing a policy to implement an extension of the training requirement on the responsible conduct of research (RCR) to all persons supported by PHS research. The protection of human subjects in research will be included in the RCR institutional assurance. A draft of this policy will be posted for comment on the ORI website in June, 2000.

Educational Resources: While all investigators need education in the basics of human subjects research, some may elect more intensive study if their work involves especially difficult topics or special populations. Many institutions already have developed educational programs on the protection of research participants and have made participation in such programs a requirement for their investigators. The NIH does not plan to issue a list of "endorsed" programs. Rather, the NIH points out that a number of curricula are readily available to investigators and institutions. For example, all NIH intramural investigators and research administrators who oversee clinical projects are required to complete an on-line tutorial on the protection of human research subjects. This training can be accessed on the web site of the NIH Office of Human Subjects Research at http://ohsr.od.nih.gov/. While this training module was developed for NIH staff, it can be used by other institutions seeking to meet training requirements in this area.

To facilitate education and the development of curricula, the NIH launched a website on bioethics in 1999. (See http://www.nih.gov/sigs/bioethics/)This site is replete with resources (>4500 references) on a broad range of relevant topics, including human subjects in research, medical and healthcare ethics, and the implications of genetics and biotechnology. This website also contains a broad set of annotated web links, including some attached to training programs. In addition, the University of Rochester has made available its training program for individual investigators. Their manual can be obtained through CenterWatch, Inc. (http://www.centerwatch.com).

To address longer-term needs, the NIH has two program announcements to support training on ethical issues related to research and human subjects. The first announcement provides support (T15) for institutions to conduct short-term courses in research ethics. (See http://grants.nih.gov/grants/guide/pa-files/PA-99-051.html) The primary objectives of the T15 program are to increase knowledge among investigators regarding research ethics and to protect human participants in clinical protocols. The second announcement supports career development of individuals who are committed to a career in research ethics. These individuals will be able to serve as resources in the institutions and as catalysts in discussions of critical ethical issues in research. (See http://grants.nih.gov/grants/guide/pa-files/PA-99-050.html).

Attachment #2

REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS

Release Date: September 5, 2001

NOTICE: NOT-OD-01-061

National Institutes of Health

Policy: Beginning on October 1, 2000, NIH implemented a policy requiring education on the protection of human research participants for all key personnel submitting NIH applications for grants or proposals for contracts or receiving new or non-competing awards for projects involving human research participants (see June 5, 2000 NIH Guide Notice).

Before funds are awarded for applications or contract proposals involving human subjects, documentation must be submitted that all key personnel have received training in the protection of human subjects. In a follow-up to the June 5, 2000 Guide Notice, it was announced that the letter documenting completion of the education required signatures of both the official authorized to represent the applicant institution and the principal investigator. In an effort to streamline the submission of the required documentation, NIH staff will now accept a letter signed by the official authorized to represent the institution. It is not required that the principal investigator also sign the letter. The letter should continue to be submitted in accordance with Just-in-Time procedures.

The education requirement also applies to key personnel at consortium institutions or performance sites if they are participating in research that involves human subjects. If the grantee organization is having difficulty obtaining this documentation, NIH staff may consider issuing awards that restrict the third party participation until the documentation has been received. This will streamline issuing awards in situations where the third party participation is not essential to the start of the project.
