



Office for Human Research Protections  
The Tower Building  
1101 Wootton Parkway, Suite 200  
Rockville, Maryland 20852  
Telephone: 240-453-8120  
FAX: 240-453-6909  
E-mail: Lisa.Rooney@hhs.gov

April 21, 2011

Robert E. Burke, CPA  
Managing Director  
Research Foundation for Mental Hygiene  
Riverview Center  
150 Broadway  
Menands, NY 12204

Dear Mr. Burke:

Thank you for your March 2, 2011 letter in response to our February 14, 2011 questions and concerns letter. We acknowledge the responses provided and the steps taken to modify or clarify language in a number of Research Foundation for Mental Hygiene (RFMH) & New York State Department of Mental Hygiene (DMH) institutional review board (IRB) manuals. These actions adequately address the questions and concerns noted in our February 14, 2011 letter.

In addition to resolving the questions and concerns that were previously raised, we make the following recommendations -- most of which involve clarifying, correcting, including, or making explicit language regarding the regulatory provisions in one or more of the RFMH/DMH Facility IRB manuals. Please note that you are not required to adopt these recommendations.

A. Recommendations Regarding the Central RFMH/DMH IRB Manual (Central IRB Manual):

1. Section 3.1 - Basis for Approval. We note that you have included all of the IRB approval criteria outlined in Department of Health and Human Services (HHS) regulations at 45 CFR 46.111(a), but did not include language contained in HHS regulations at 45 CFR 46.111(b), which states that when some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects. We recommend that you include this statement so that the IRB approval criteria are complete.
2. Section 3.2 - Review Procedures. According to this section (as well as other RFMH/DMH Facility IRB Manuals) the IRB is required to notify only investigators (in writing) of its decision to approve or disapprove a proposed research activity, or of

modifications required to receive IRB approval of a research activity. Please note that HHS regulations at 45 CFR 46.109(d) require that an IRB notify both investigators **and the institution** in writing of its decision to approve or disapprove a proposed research activity, or of modifications required to secure IRB approval of a research activity. While it is clear that each RFMH/DMH facility is notified in writing of IRB approvals, it is unclear whether each RFMH/DMH facility is notified in writing of an IRB decision to disapprove a proposed research activity or of modifications required to secure IRB approval of a research activity. Thus, as currently written this section – as well as section 6.4 of the Central IRB Manual - is not explicitly in accordance with HHS regulations at 45 CFR 46.109(d). We recommend that you modify these sections of the Central IRB Manual as well as all RFMH/DMH Facility IRB Manuals accordingly.

3. Section 3.2.1 - Federal Exempt. We note that the following language, which appears at the end of the exempt categories list, no longer appears in the HHS regulations at 45 CFR 46.101(b): “If, following review of proposed research activities that are exempt from these regulations under 46.101(b)(6) the Secretary (DHHS) determines that a research or demonstration project presents a danger to the physical, mental or emotional well-being of a participant or subject of the research or demonstration project, then federal funds may not be expended for such a project without the written informed consent of each participant or subject.” In addition, we note that the guidance provided in the footnote noted at the end of this section is no longer correct. Please note that as of June 23, 2005, the exemptions at 45 CFR 46.101(b) may apply to research involving fetuses, neonates, pregnant women or human in vitro fertilization. We recommend that you modify this section of the Central IRB Manual accordingly.
4. Section 3.7 – Approval Process for Amendments to Previously Approved Protocols. We note that the Central IRB Manual provides the following in reference to minor amendments: “Minor amendments do not increase the level of risk to patients/subjects and do not involve invasive procedures (including x-rays). Minor amendments do not include any procedures for which a full board review is necessary. Dose increases in investigational drug studies and dose increases above PDR recommended dosages for marketed drugs are not minor amendments under any circumstances.” While the Central IRB Manual provides such a definition, we note that none of the RFMH/DMH facility IRB manuals include the same definition. For example, we could not find any definition for minor vs. more than minor amendments in the Nathan S. Kline Institute IRB Manual (NSKI IRB Manual), the Institute for Basic Research IRB Manual (IBR IRB Manual), the Bronx Psychiatric Center IRB Manual (Bronx IRB Manual), etc. As a result, we recommend that the RFMH/DMH facility IRBs adopt the same or a similar definition for minor amendments.
5. Section 3.8 - Reporting Requirements. This section of the Manual lists three items that the principal investigator is responsible for promptly reporting to the IRB. We note that this list is incomplete in that it does not state that a principal investigator is responsible for reporting serious or continuing noncompliance as required by 45 CFR 46.103(b)(5). We recommend that you modify this section so that it is complete.

6. Section 4.7 – Retention of Signed Consent Documents. Per this section, when research has been completed, the investigator should seek the advice from the IRB and legal staff about the need to retain signed consent documents, and as a general rule, a period of three years following completion of the research is **recommended** for social science research and three to fifteen years for medical research. Please note that HHS regulations at 45 CFR 46.115(b) require institutions to retain records of IRB activities and certain other records frequently held by investigators – including signed consent documents - for at least three years after completion of the research unless the IRB waived the requirement for informed consent (under 45 CFR 46.116(c) or (d)) or the requirement for documentation of informed consent (under 45 CFR 46.117). Given this explanation, we recommend that you change the language noted above accordingly.

B. Recommendations Regarding the New York State Psychiatric Institute IRB Manual (NYSPI IRB Manual):

1. Section 6 – Procedures for Review. According to this section, new research involving data analysis, records review, survey research and other low risk, low complexity research is reviewed by the Chair. Notwithstanding this statement, we note that the NYSPI IRB Manual does not include procedures specific to expedited review. We recommend adding a section describing expedited review procedures.
2. Section 6.x – Minutes. We note that this section of the NYSPI IRB Manual includes all of the regulatory required details for maintaining IRB meeting minutes except the basis for disapproving research. See 45 CFR 46.115(a)(2). We recommend that you modify this section to include this regulatory requirement.
3. Section 6.3.f.ii – Expedited Review. This section provides that “Review and approval of minor changes in previously approved research during the period (of one year or less) for which IRB approval is authorized may be conducted under an expedited review procedure in accordance with 45 CFR 46.102(i).” Please note that the regulatory provision cited is incorrect: 45 CFR 46.110 is the regulatory provision which addresses expedited review. Moreover, we note that this section provides that [expedited] review and approval may be carried out by the IRB Chair, an IRB Subcommittee, or less commonly, may be delegated to an IRB member. Please note that under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers, designated by the chairperson from among members of the IRB. See 45 CFR 46.110(b). Thus, please ensure that the IRB member(s) that are conducting expedited reviews on behalf of the NYSPI IRB are experienced reviewers, who have been designated by the chairperson from among members of the IRB.

C. Recommendations Regarding the NSKI IRB Manual:

1. Section C – Membership and Meetings. As you may be aware, HHS regulations at 45 CFR 46.107(e) do not permit an IRB member to participate in the initial or continuing review of any project for which they have a conflicting interest, except to provide information requested by the IRB. IRB members who have a conflict with a particular

project are not permitted to participate in the voting for such a project and do not count toward the quorum for the project for which they have a conflicting interest.

According to the NSKI IRB Manual (as well as other RFMH/DMH facility IRB manuals, e.g., IBR IRB Manual, Office of Mental Health IRB Manual (OMH IRB Manual), the Bronx IRB Manual, etc.), it appears that an IRB member with a conflicting interest in a study is counted as an “abstention” for the vote for the study and, by extension, his/her presence is counted towards quorum. Please note that this guidance is not accurate in that IRB members with a conflicting interest in a project are counted as “recusals” for that vote and their presence does not count toward quorum for the project. We recommend that the NSKI IRB manual, as well as all other IRB manuals, be modified accordingly.

2. Section C – Membership and Meetings. We note that the NSKI IRB, as well as other RFMH/DMH facility IRB Manuals, lists five options the convened IRB can take on a submitted protocol. We recommend that you review our recently released guidance document entitled Guidance on IRB Approval of Research on Conditions, available at <http://www.hhs.gov/ohrp/policy/conditionalapproval2010.html>, for guidance regarding when a protocol can be approved with conditions and when a protocol can not be approved because the IRB cannot make one or more of the determinations required for approval by the HHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46.
3. Section F.1 – Continuing Review. According to this section, if the continuing review application is not approved by the IRB in a timely manner, the IRB approval for the study must be suspended and all subject accrual must stop, until such time as a Continuing Review report is submitted and approved by the IRB. (Continuation of research interventions in already enrolled subjects will only be permitted when the IRB finds that it is in the best interests of individual subjects to do so.) Please note that if a continuing review application is not approved by the IRB in a timely manner, all non-exempt human subjects research activities – not just subject accrual - must cease until such time as a Continuing Review report is submitted and approved by the IRB unless it is in the best interests of subjects to continue. For example, no data analysis of private identifiable information or research-related surveys/questionnaires may occur during this time. We recommend that you revise this section accordingly.
4. Section G – Submission of Protocols. We note that according to the NYSI Manual “If an application to a granting agency or foundation has been prepared, the application may be provided to the IRB instead of preparing a separate protocol.” Please note that this process is acceptable as long as the grant application includes a comprehensive description of the proposed research project, including information about the proposed research that is typically required by the NSKI IRB in its instructions to investigators for submitting projects to the IRB for review. In many cases, a grant application that contains the above-mentioned information and is provided to the IRB may be considered adequate.

Although we have not previously posted this guidance on our website, we believe that if a grant application (or any other combination of documents, e.g., a protocol summary and informed consent document) includes sufficient information upon which an IRB can make the 45 CFR 46.111 approval determinations, then the IRB could rely solely on such a document when making the required findings. Alternatively, if the grant application, or any other combination of documents, does not provide sufficient information upon which an IRB can make the applicable 45 CFR 46.111 approval determinations, then the IRB would need to solicit additional information so that the IRB could make such determinations; this information could come from a variety of sources, including the complete protocol or email communications from the investigator. Please note that for HHS-supported research, the IRB (that is designated to review for the prime awardee institution) must receive and review the grant application.

We believe it may be more likely that an IRB could rely on a grant application when making approval determinations for minimal risk or less complex research, because it seems more likely that the grant application would contain sufficient information for an IRB to make the findings under 45 CFR 46.111. For example, it would be reasonable for an IRB to rely on the grant application when reviewing a blood draw study; the expectation being that those documents, alone or in combination with additional information, would provide sufficient information upon which an IRB could make the required determinations. Alternatively, in most cases we do not believe an IRB could rely on only a grant application when making approval determinations for greater than minimal risk or more complex research. We believe that for such research, the various features of the proposed research that the IRB would need to take into consideration in making its determinations would be considerable and that the complete protocol is likely to be the only document that would contain all of the relevant information upon which an IRB could make the required regulatory determinations. We are concerned that if an IRB relies only on the grant application for such research, the IRB runs the risk that relevant information contained in the full protocol: (a) may be omitted from the grant application, either by mistake or intention; or (b) may be inappropriately communicated in the grant application and that this omitted or inappropriately communicated information may have a bearing on whether an IRB could make 45 CFR 46.111 approval determinations.

We recommend that IRBs follow our Guidance on Written IRB Procedures – available at <http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd107.htm> – which reflects our current thinking on this matter. Of note, this document provides that when conducting the initial review of proposed research, an IRB must obtain information in sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111. The guidance document states that the materials to be reviewed to make the 45 CFR 46.111 findings should include the full protocol, a proposed informed consent document, any relevant grant application(s), the investigator's brochure (if one exists), and any recruitment materials, including advertisements intended to be seen or heard by potential subjects. For HHS-supported multicenter clinical trials, the IRB should also receive and review a copy of the HHS-approved sample informed consent document and the complete HHS-approved protocol, if they exist. Unless a primary reviewer system is used, all members should receive a copy of the documentation noted above. Conversely,

if an IRB uses a primary reviewer system, the primary reviewer(s) should do an in-depth review of all pertinent documentation noted above. All other IRB members should at least receive and review a protocol summary (of sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111), the proposed informed consent document, and any recruitment materials, including advertisements intended to be seen or heard by potential subjects.

D. Recommendations Regarding the Bronx IRB Manual:

Section G.6 – Waiver or Alteration of Consent. Per this section, in order for the Bronx IRB to waive or alter informed consent, the IRB will find and document that the research meets the waiver criteria delineated at 45 CFR 46.116(c) or (d), and that the IRB will specifically record such waivers of consent and appropriate findings in its meeting minutes. However, we note that according to the March 19, 2010 Bronx IRB Meeting Minutes the Bronx IRB waived informed consent for study 10-01, but failed to specifically record its findings in its meeting minutes. Of note, the only reference to waiver of consent is as follows: “Vote to approve study, including the HIPAA Waiver/Waiver of Consent: Total votes – 8; votes for – 8, votes opposed – 0, abstained – 0.” The IRB meeting minutes do not address whether and how the study meets the 45 CFR 46.116(c) or (d) criteria. As the documentation of the IRB’s findings is a regulatory requirement under 45 CFR 46.116(c) and (d), please ensure that in the future the Bronx IRB documents the appropriate findings.

E. Recommendations Regarding the Sagamore Children’s Psychiatric Center/Queens Children’s Psychiatric Center (SCPC/QCPC) IRB Manual:

Section H – Research Involving Children. We note that this section of the manual states that “The Minutes of the IRB meeting will document under which of the four regulatory categories a study involving children is approved.” Notwithstanding this statement, we note that the IRB meeting minutes dated March 12, 2010 did not include this information. We recommend that you ensure that the IRB is following its procedures.

Given that you have adequately resolved the questions and concerns noted in our February 14, 2011 letter, there should be no need for further involvement by our office in this matter.

We appreciate your institution’s continued commitment to the protection of human research subjects.

Sincerely,

Lisa A. Rooney, J.D.  
Compliance Oversight Coordinator

Cc: Ms. Susan J. Delano, CIP, Deputy Managing Director, RFMH  
Dr. David Strauss, Chair, RFMH IRB#1 and IRB#4  
Dr. Abel Lajtha, Chair, RFMH IRB#2  
Dr. Edmund Jenkins, Chair, RFMH IRB#3  
Ms. Sheila Donahue, Chair, RFMH IRB#5  
Dr. Jennifer Berryman, Chair, RFMH IRB#6  
Dr. Daniel Pharr, Chair, NY State Office of Mental Health (NYSOMH) IRB#7  
Mr. Daniel Woodcock, Chair, RFMH IRB#9  
Dr. Louis Linfield, Chair, NYSOMH IRB#11  
Dr. Maureen Empfield, Chair, RFMH IRB#17  
Ms. Maxine Block, Chair, RFMH IRB#18  
Dr. Deborah Hall, Chair, RFMH IRB#19  
Dr. Thomas Uttaro, Chair, RFMH IRB#20  
Dr. William Ansorge, Chair, RFMH IRB#21  
Dr. Jerome Meyer, Chair, NYSOMH IRB#27  
Dr. James McCarthy, Chair, RFMH IRB#41  
Dr. Roger Christenfield, Chair, RFMH IRB#42  
Dr. Margaret Hamburg, Commissioner, Food and Drug Administration (FDA)  
Dr. Joanne Less, FDA  
Dr. Sherry Mills, Office of Extramural Research (OER), National Institutes of Health (NIH)  
Dr. Joe Ellis, OER, NIH