Appendix B

Documentation of Evaluation Greer Study Compliance With the Common Rule

RESEARCH SUPPORT OFFICE
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To:	Andrea Wullenweber	**Fax:**	513-542-7487
From:	Charlotte Shupert	**Date:**	2/14/2002
Phone:	503-494-9644 **Fax:** 503-494-7787	**Pages:**	3
CC:		**Re:**	Requested materials

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IRB letter as requested. Original is in US Mail.

Charlotte L. Shupert, Ph.D.
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February 14, 2002

Andrea Wullenweber, M.S.
Toxicology Excellence for Risk Assessment (TERA)
1757 Chase Avenue
Cincinnati, OH 45223

Dear Ms. Wullenweber:

I am writing to respond to your inquiry about the membership of the OHSU Institutional Review Board that completed reviews for Dr. Monte Greer's protocol, "Study of Perchlorate Pharmacokinetics and Inhibition of Radioactive Iodine Uptake (RAIU) by the Thyroid in Humans," during the period of January 1 through June 30, 2000.

OHSU conducts all research according to the terms of our federal assurances. During that time, OHSU operated under a Multiple Project Assurance (M1359). Since March 2001, we have operated under a Federal-Wide Assurance (FWA00000161). Both during the period of the MPA and the FWA, our Institutional Review Boards have been constituted according to the requirements set out in 45 CFR 46.

Attached please find a board roster with names, affiliations, and areas of expertise for the OHSU IRB for this study at that time.

Yours truly,

Charlotte L. Shupert, Ph.D.
Compliance Manager

Oregon Health & Science University

Institutional Review Board Roster for
January–June, 2000

Name	Expertise	Affiliation
Bigelow, D. Ph.D.	Psychology	OHSU
Casson, H. M.D.	Anesthesiology	OHSU
Cereghino, J. M.D.	Neurology	OHSU
Chiodo, G. D.M.D. (CHAIR)	Dentistry	OHSU
Hansen, S. M.D.	Internal Medicine	OHSU
Lepley, E. J.	Counseling	Unaffiliated
McKenzie, Darlene	Nursing	OHSU
Menashe, V. M.D.	Pediatric Cardiology	OHSU
Moneta, G. M.D.	Vascular Surgery	OHSU
Morris, J. M.D.	Pulmonology	OHSU
Munar, M., Pharm.D.	Pharmacology	OHSU
Pratt, C. Ph.D., J.D.	Law	Unaffiliated
Riddle, E. D.M.	Theology	Unaffiliated
Riviere, G. Ph.D., D.D.S.	Dentistry	OHSU
Shupert, C. Ph.D.	Neuroscience	OHSU

Perchlorate (CRC #628)

Materials Reviewed:

"Study of Perchlorate Pharmacokinetics and Inhibition of Radioactive Iodine Uptake (RAIU) by the Thyroid in Humans" Protocol CRC #628. 8 February 2000.

Key Documents Reviewed:

Protocol and amendments
- February 2000 protocol (main study)
- May 2000 protocol (uptake only study)

Ethics Committee approvals and composition of ethical committee
- Protocol approval date 2/1/00 (IRB # 5798)
- Memorandum 2/11/00
- Project revision amendment administrative approval 4/12/00
- Oregon Health Sciences University (OHSU) 2000 Institutional Review Board Policy and Procedure Manual
- Letter from OHSU to *TERA* regarding federal assurances and IRB roster 2/14/02

Sample written information for subjects and consent form
- Consent Forms (dated, 2/1/00, 4/12/00, 5/5/00)
- Protocol requirements spreadsheets (verify signed informed consent forms)

Sponsor: The Perchlorate Study Group

Laboratory: Oregon Health Sciences University (OHSU)

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How *TERA* Conducted This Evaluation

TERA was asked to answer the question "Has this human study met the criteria as established under the Common Rule for the ethical treatment of human subjects?" To answer this question, *TERA* identified key elements of the Common Rule and then evaluated the provided documentation for the study to determine whether the key elements were met. Note that some elements of the Common Rule are substantive, while others are procedural. An evaluation of this type lends itself to more of the procedural items being identified and checked off. We have identified those elements with which we could document compliance. However, if the information reviewed does not specifically address an item, that does not necessarily mean that the study was conducted improperly, it may just mean that *TERA* did not have documentation upon which to base an assessment.

Common Rule (CR) Elements (40 CFR 26)	**Oregon Health Sciences University Perchlorate**
Purpose The "Common Rule" is a **policy** that applies to all research involving human subjects that are conducted, supported, or otherwise "subject to regulation" by any federal department or agency. EPA limits the application of the Common Rule to studies conducted or funded by EPA.	"All requirements of 45 CFR 46[6] will be met for all applicable DHHS [Department of Health and Human Services] -supported research, and all other human subject research regardless of sponsorship, except as otherwise noted in this Assurance. Federal … funds for which the Assurance applies may not be expended for research involving human subjects unless the requirements of this assurance have been satisfied." (chpt. 1, p. 2)[7] OHSU submitted a letter to *TERA* indicating that it conducts all research according to the terms of its federal assurances. During the time of this study, OHSU operated under a Multiple Project Assurance (M1359).
Applicability of the CR **§26.101(a)** – This policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research. **§26.101(b) --** provides exemptions to policy. **§26.101(h)** – When research covered by this policy takes place in foreign countries, procedures normally followed in foreign countries to protect human subjects may differ from those set forth in this policy (e.g., guidelines consistent with the Declaration of Helsinki amended 1989). In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the provisions set forth in the CR.	*NA for this study, as it was not federally funded. However, OHSU 2000 IRB Policy and Procedures Manual states that "Federal … funds for which the Assurance applies may not be expended for research involving human subjects unless the requirements of this Assurance have been satisfied." (chpt. 1, p. 2)* NA. Study conducted in United States.
Requirements of the CR **§26.111(a)(4) –** Investigators must receive informed consent from human subjects participating in the proposed study. **§26.107 –** An IRB must be established. The term IRB is defined in **§26.102(g)** as an institutional review board that must be established for review of human research subject to the CR. **§26.103 –** CR requires that institutions engaged in research involving human subjects and conducted	Informed consent specified in protocol and verified in Protocol Requirements Spreadsheet. *"The OHSU IRB is… charged with protecting the rights and welfare of human subjects recruited to participate in research activities conducted under the auspices of OHSU. (chpt. 2, p. 6)* Written assurance not applicable to this study as it was not conducted nor supported by a Federal

[6] Note that 45 CFR 46 is the Department of Health and Human Services regulations for the Common Rule.

[7] Citations are from OHSU 2000 IRB Policy and Procedures Manual unless otherwise noted.

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or supported by a Federal department or agency provide written assurance deemed acceptable by the department or agency that the institution will comply with the requirements set forth in the CR (including designation of an IRB and the establishment of written procedures for the IRB) and provide certification of compliance.	department or agency. However, during the time of the study, OHSU operated under a Multiple Project Assurance (M1359).
IRB Functions and Operations **- §26.108(b)** – to review proposed research at convened meetings at which a majority of members are present, with at least one member whose primary concerns are in nonscientific areas. Approval of proposed research requires a majority of the members present at the meeting.	The protocol and consent form were approved by the OHSU IRB on February 1, 2000.
IRB Membership –	
§26.107(a) – required minimum of five members of varying backgrounds. **§26.107(b)** – no IRB can be entirely made up of members of one gender or one profession. **§26.107(c)** – IRB must have at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are nonscientific areas. **§26.107(d)** – IRB must have at least one member not otherwise affiliated with the institution performing, supporting, or regulating the proposed research.	"The OHSU IRB consists of a Chair, 30 primary members, and 6 alternates. Five primary members represent the public. The other members are OHSU faculty who represent a wide range of professional backgrounds and experience in research and ethics." (chpt. 2, p. 6) "One more than half of the IRB members must attend meetings including the Chair or Vice Chair to achieve a quorum to conduct official IRB business. (chpt. 6, p.13) The IRB roster and protocol approval letter indicate that both genders, at least one lay person, and more than one profession were included.
§26.107(e) – no IRB may have a member participating in initial or continuing review of any project in which the member has a conflicting interest.	"No OHSU IRB member may participate in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB." (chpt.6, p.13)
§26.107(f) – IRB may invite individuals with competency in specialized areas in the review of projects involving expertise beyond that of the IRB members. These individuals may not vote with the IRB.	Yes (written practically verbatim). (chpt. 6, p. 13).
IRB Review and Approval of Research, and Ongoing Review **§26.109(a)** – An IRB is required to review and has the authority to approve, require modifications in, or disapprove all research activities covered by the CR.	Yes (written practically verbatim). (chpt. 4, p. 9 and chpt. 8, p. 17) "This review will be in compliance with 45 CFR 46 and provisions of multiple project assurance unless the project is determined to be exempt by the IRB chair." (chpt. 4, p. 9)
§26.109(d) – An IRB must provide written notification to the investigator(s) and institution	Yes (written practically verbatim). (chpt. 8, p. 17)

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regarding its decision to approve or disapprove the proposed research or of any modifications required for approval.	
§26.109(e) – An IRB must also conduct continuing review of research covered by the CR at intervals appropriate to the degree of risk associated with the study, but not less than once per year.	Yes (written practically verbatim). (chpt. 8, p. 17)
§26.110(b) – An IRB may use expedited review procedures to review either or both of the following: (1) Some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk;	Yes. Specifies that expedited review to be conducted in accordance with requirements of 45 CFR 46.110 and provides detailed list of types of research that would be eligible for expedited review when the research involves no more than minimal risk to human subject. Also identifies types of research that would be eligible for exemption from review (if meets 45 CFR 46.101) (chpt. 9, pp. 21-25)
(2) Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.	Yes. States that may use expedited review to review minor changes in ongoing previously approved research during the period for which approval is authorized. (chpt. 11, p. 40)
Criteria for IRB Approval of Research **§26.111(a)(1) through (a)(7) –** An IRB may not approve research subject the CR unless it determines that all of the proposed research satisfies the following requirements: • **Risks to subjects are minimized** by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes. • **Risks to subjects are reasonable** in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. • **Selection of subjects is equitable**, taking into account the purposes of the research and the setting in which the research will be conducted, and the special problems of research involving vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or otherwise economically or educationally disadvantaged persons. • **Informed consent** has been sought, obtained from subjects and documented in accordance with the CR. • When appropriate, the research plan makes adequate provision for monitoring the data	Yes. These criteria are listed in OHSU 2000 IRB Policy and Procedure Manual. (chpt. 8, p. 17)

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collected to **ensure the safety of subjects**. • When appropriate, there are adequate provisions in the research plan to **protect the privacy of subjects** and maintain confidentiality of data. **§26.111(b) –** When some or all of the subjects are likely to be vulnerable to coercion or undue influence, the IRB must ensure that additional safeguards have been included in the study to protect those individuals.	Yes. Listed along with the criteria above. (chpt. 8, p. 17)
IRB Procedural Requirements **§26.103(b)(4) –** Written procedures that the IRB will follow must be documented as part of the assurance of compliance with the CR. These procedures relate to the following: (i) conduct of initial and continuing review of research and reporting its findings and actions to the investigator and the institution; (ii) determination of which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) ensuring prompt reporting to the IRB of proposed changes in a research activity, and ensuring that such changes in approved research may not be initiated without IRB approval except when necessary to eliminate apparent immediate hazards to the subject.	Yes. Included in OHSU 2000 IRB Policy and Procedure Manual. (chpt. 8, pp. 17-18)
§26.103(b)(5) – Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval.	Yes. Included in OHSU 2000 IRB Policy and Procedure Manual. (chpt. 8, p. 18)
Review by Institution **§26.112 –** Research subject to the CR that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. Such officials, however, may not approve research not approved by an IRB.	
Documentation of IRB Activities **§26.115(a) and (b) –** An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities including: (1) copies of research proposals reviewed, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects; (2) minutes of IRB	Yes. Included in OHSU 2000 IRB Policy and Procedures Manual. (chpt. 10, pp. 30-31)

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meetings with the detail specified in **§26.115(a)(2)** of the CR; (3) records of continuing review activities; (4) copies of all correspondence between the IRB and the investigator(s); (5) list of IRB members; (6) the written procedures for the IRB; and (7) statements of significant new findings provided to subjects. Records required by the CR must be retained for at least 3 years, and records relating to the research being conducted must be retained at least three years after completion of the research.	
General Requirements for Informed Consent **§26.116 –** For research projects subject to the CR, investigator(s):	
• Must obtain legally effective informed consent from any human subject or the subject's legally authorized representative.	Yes. Informed consent must be sought from each prospective subject in accordance with 45 CFR 46. (chpt. 11, p. 34)
• Must seek consent only under circumstances that provide the prospective subject or representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.	Protocol states that "To further assure informed consent, at the Preliminary Visit all potential volunteers will be asked to take home the materials provided and to phone the next day with their decisions concerning participation. Informed consent will be documented by having the volunteer sign the consent form in front of the principal investigator." Consent form indicates that "…participation of OHSU students in OHSU research is completely voluntary and you are free to choose not to serve as a research subject in this protocol for any reason. If you do elect to participate… you may withdraw from the study at any time without affecting your relationship with OHSU, the investigator, the investigator's department, or your grade in any course." (Consent Form, p. 3).
• Must provide information to the prospective subject that is expressed in understandable language.	The consent form is written in understandable language.
• Must not include any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights, or language that releases or appears to release the investigator, the study sponsor, the institution, or its agents from liability for negligence.	Does not include exculpatory language. Specific guidance for procedures in case of subject suffering is spelled out. Consent form states, "You have not waived your legal rights by signing this form." (Consent Form, p. 3)
The same section sets forth statements that must be provided to subjects regarding informed consent:	
• A statement that the study involves research, an explanation of the purposes of the research, and the expected duration of the subject's participation, a description of the procedures to	Yes. Each item is included in the Consent Form.

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be followed, and identification of any procedures which are experimental. • A description of any reasonably foreseeable risks or discomforts to the subject. • A description of any benefits to the subject or to others that may reasonably be expected from the research. • A disclosure of appropriate alternative procedures or courses of treatment, if any, that may be advantageous to the subject. • A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. • For research involving more than minimal risk, an explanation as to whether any compensation and any medical treatments are available if injury occurs, and, if so, what they consist of, or where to obtain additional information. • An explanation of whom to contact for answers to questions about the research and the subjects' rights and whom to contact in the event of a research-related injury to the subject. • A statement that participation is voluntary, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.	
• When appropriate, one or more additional enumerated elements of informed consent shall be provided to each subject as specified in **§26.116(b)**, including: (1) a statement that the particular treatment or procedure may involve risks to the subject (or the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable; (2) anticipated circumstances under which the subject's participation may be terminated with subject's consent; (3) any additional costs to the subject resulting from participation; (4) the consequences of a subject's decision to withdraw and procedures for orderly termination of participation by the subject; (5) a statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue in the research will be provided to the subject; and (6) the approximate number of subjects in the study.	Yes. Each of these items is included in IRB Policy and Procedures Manual, except identifying approximate number of subjects in the study. (chpt. 11, p. 34-36)
§26.116(c) and (d) outline circumstances when informed consent may be waived or which may be altered.	Yes. Included in OHSU2000 IRB Policy and Procedures Manual. (ch. 9, pp. 25-28)

Common Rule (CR) Elements (40 CFR 26)	**Oregon Health Sciences University Perchlorate**
	Informed consent was required for this study.
Documentation of Informed Consent **§26.117(a) through (c) –** The investigator(s) must document informed consent as follows:	
• Informed consent must be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's authorized representative, and a copy must be provided to the person signing the form.	Yes. Written consent form approved by IRB. Consent form includes a statement that subject shall receive a copy of consent form.
• Either a long or a short form written consent document may be used, under the specified conditions, as described below.	Long form. Consent form contains all elements (except number of subjects in study).
• The long form must include the elements of informed consent required by the CR. While this form may be read to the subject or representative, the investigator must give either the subject or the representative adequate opportunity to read the form before it is signed.	Protocol states that "To further assure informed consent, at the Preliminary Visit all potential volunteers will be asked to take home the materials provided and to phone the next day with their decisions concerning participation. Informed consent will be documented by having the volunteer sign the consent form in front of the principal investigator." (Consent Form, p. 3)
• If the short form is used, it must state that the elements of informed consent required by the CR have been presented orally to the subject or the subject's legally authorized representative. When the short form is used, there must be a witness to the oral presentation and the IRB must approve a written summary of what is to be orally stated to the subject or the representative. While only the short form itself is to be signed by the subject or representative, the witness must sign both the short form and a copy of the summary, and the person actually obtaining consent must sign a copy of the summary. A copy of both the short form and the summary must be given to the subject or representative.	NA, short form not used.
• An IRB may waive the requirement for signed consent form under certain conditions outlined in **§26.117 (c).**	NA. Consent form required for this study.
Written Assurance **§26.103(a) through (f) –** Each institution engaged in research that is covered by the CR and is conducted or supported by a Federal department or agency must provide written assurance satisfactory to the department or agency head that the institution will comply with the requirements set forth in the CR. Among other things, the assurance must include:	OHSU submitted a letter to *TERA* indicating that it conducts all research according to the terms of its federal assurances. During the time of this study, OHSU operated under a Multiple Project Assurance (M1359).
• A statement of principles governing the institution with regard to protecting the rights and welfare of human subjects of research.	
• Designation of one or more IRBs established in	

Common Rule (CR) Elements (40 CFR 26)	**Oregon Health Sciences University Perchlorate**
accordance with the CR, with an identification of IRB members and a description of relevant backgrounds. • The written procedures which the IRB must follow. The regulations specify in detail the required contents of these procedures, including those that ensure prompt reporting of any unanticipated problems with the research involving risks to human subjects. • The department or agency head will take into consideration a number of factors, including the adequacy of the proposed IRB in light of the anticipated scope of research activities, in determining whether to approve or disapprove the assurance or enter into negotiations for an approvable assurance. An institution with an approved assurance must certify that each application or proposal for research covered by the assurance and not exempted or waived has been reviewed and approved by the IRB.	