DEPARTMENT OF HEALTH & HUMAN SERVICES

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October 24, 2002

Peter O. Kohler, M.D.
President
Oregon Health & Science University
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Portland, OR 97201-3098

RE: Human Research Protections Under Federal Wide Assurance FWA-161

Research Project: Student Athlete Drug Surveillance Trial (SATURN)
Principle Investigator: Linn Goldberg, M.D.
OHSU IRB Number: 4682
HHS Protocol Number: R01DA012018

Dear Dr. Kohler:

As you know, the Office for Human Research Protections (OHRP) conducted an on-site evaluation of human subject protection procedures at the Oregon Health & Science University (OHSU) on October 2-4, 2002. While OHRP issued determinations on October 4, 2002 regarding general human subjects protections at OHSU, OHRP was not prepared at that time to present findings related to the SATURN study.

At this time, OHRP makes the following determinations regarding the SATURN study.

(1) OHRP finds that mandatory drug testing of student athletes is an integral part of the design of the SATURN research protocol. OHRP finds that the principal investigator designed a research study in which the goals of mandatory drug testing of student athletes and the scientific aims of the study are so closely interwoven as to be indistinguishable. The particular nature of the study design may have prevented both the OHSU Institutional Review Board (IRB) and the investigators from clearly recognizing that the drug testing is an integral part of the study. OHRP's conclusion that the mandatory drug testing of student athletes is part of the study design is supported by the following observations:

(a) The specific aims stated in the IRB- approved research protocol included the evaluation of the drug testing.

(b) The IRB-approved protocol included detailed descriptions of the drug testing.

(c) The study design relies on a randomized intervention, i.e., randomization of groups of student athletes by school to either mandatory drug testing or to no drug testing. The principal investigator acknowledged during the interview with the site visit team that the study was an intervention study.

(d) The co-investigator acknowledged during the interview with the site visit team that the drug testing is integral to the research project. She also acknowledged that the investigators needed to control the drug testing methodology to ensure the success of the protocol. This need to control all facets of the drug testing for the sake of the SATURN research study is readily apparent in multiple communications between the research team and the participating school districts.

(e) The director of the drug testing lab is identified in the grant application as professional staff for the protocol, and elsewhere as a research collaborator.

(f) The investigators strongly influenced school drug testing policy. Most, if not all, of the schools participating in the SATURN study had no drug testing policies prior to being approached by the SATURN investigators. Several schools had not even considered drug testing athletes until approached by the SATURN investigators. At least one school had considered drug testing of athletes, but could not implement such testing prior to participating in the research, mostly due to cost considerations. The SATURN investigators provided sample drug testing policies to the schools, which, even if these policies were open to some modification by the schools, placed the investigators in a policy-setting role.

(g) The investigators are physically involved in the collection of the drug test samples and serve as the initial recipients of the drug test results, which are then relayed to the schools.

(h) The SATURN project pays for the drug testing.

(2) HHS regulations at 45 CFR 46.116 require, among other things, that the investigator shall seek informed consent only under circumstances that minimize the possibility of coercion or undue influence. OHRP finds that the circumstances under which subjects were enrolled and the study was conducted failed to meet this requirement. In particular, OHRP notes the following:

(a) As noted above, the mandatory drug testing of student athletes is an integral part of the SATURN research protocol design, and includes the requirement that participating schools disqualify students from athletics if they refuse to undergo the drug screening required by the research project. As a result, the research environment included the threat of being disqualified from athletics if a student did not participate in the research (which includes the drug testing), and was therefore coercive.

(b) The use of high school principals and coaches to solicit assent from their students and parental permission raises serious questions as to the perceived voluntariness of participation.

(c) The open classroom setting for distribution and completion of research surveys, in all likelihood, resulted in an undue influence for some students. Students might reasonably be expected to feel pressure to participate in the research if the majority of their peers were obviously participating. Some students may fear that they would be seen as having something to hide (e.g., drug use) if they did not participate. The principal investigator acknowledged, during the site visit interviews, the potential for peer pressure in the completion of the research questionnaires.

(d) Correspondence and interviews suggested there were monetary and practical incentives for the schools to have drug testing policies implemented via the SATURN project. Such incentives may have contributed further to an environment in which the possibility of coercion or undue influence was not minimized.

(3) HHS regulations at 45 CFR 46.103(b)(4)(iii) require that the IRB review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. OHRP finds that the following protocol changes were implemented without IRB review and approval:

(a) The investigators provided incentives to SATURN schools to encourage the collection and return of questionnaire consent forms.

(b) The investigators provided one SATURN school with a “script for phone calls” to parents urging them to sign the consent forms.

(c) The protocol stated “Positive test results will be sent from the ... laboratory to the school, and the school will send a copy to the investigator” and “a copy of the test results will be sent by school officials to the investigators only for those students who have consented to be in the study.” However, the investigator reported to the site visit team that all test results were sent to the researchers and then relayed to the schools.

(d) The protocol stated "Teachers will not be involved with data collection." However, interviews by OHRP with staff at several of the participating schools indicated that teachers handed out and collected the questionnaires at some of the schools.

(4) HHS regulations at 45 CFR 46.116 state that, except as provided elsewhere in the regulations, no investigator may involve a human being as a subject in research covered by the regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. Under HHS regulations at 45 CFR 46.408(a) and (b), the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent, and, in accordance with and to the extent that consent is required by 45 CFR 46.116, that adequate provisions are made for soliciting the permission of each child's parents or guardian for the children to participate in the research. HHS regulations at 45 CFR 46.117 and 46.408(d) require that informed consent and parental permission be documented by the use of written forms approved by the IRB and signed by the subject, the subject's legally authorized representative, or parent or guardian, unless the IRB waives these requirements in accordance with HHS regulations at 45 CFR 46.117(c). HHS regulations at 45 CFR 46.408(e) require that when the IRB determines that child assent is required, it also shall determine whether and how assent must be documented. Of note, the IRB-approved protocol for this study required that investigators document the assent of the student athletes and permission of their parents with signed assent and permission forms.

OHRP finds that the SATURN investigators initiated human subjects research without meeting these requirements for some subjects in this research. In particular, OHRP notes the following:

(a) Questionnaires were administered to some children prior to obtaining subject's written assent and parental permission, relying on student self-report of assent and permission.

(b) OHRP is concerned that some schools are providing, at the request of the project coordinator, identifiable private information (name and the fact that they do not wish to participate in the research) of non-consenting student athletes.

(c) Investigators reported that they received more questionnaires than assent and permission forms from children in the SATURN study.

(5) OHRP finds that the informed consent documents reviewed and approved by the IRB for the SATURN study failed to include or adequately address the following elements required by HHS regulations at 45 CFR 46.116(a):

(a) Section 46.116(a)(1): a complete description of the procedures to be followed, and identification of any procedures which are experimental. In particular, OHRP notes the

following:

(i) There is no statement in the informed consent document that the research involved randomization of high schools to either a prospective drug prevention efficacy arm (using random, mandatory drug surveillance and alcohol testing procedures) or no drug testing control group. Furthermore, the informed consent document may have misled subjects into thinking that the drug testing is not part of the research design.

(ii) There is no statement in the informed consent document that parents will be notified of positive drug test results.

(iii) There is no description of the "longitudinal study" as referenced in OHSU's July 11, 2001 report to OHRP. This report also stated that "[s]tudents who agree to participate but who wish to recuse themselves from the longitudinal study may complete a questionnaire anonymously... participation in the study (with longitudinal tracking) is strictly voluntary and will not impact their participation in sports or other school programs." However, this was not clearly described in the informed consent documents.

(iv) Several parts of the informed consent document for the student athletes and materials sent to their parents and schools implied that completion of the questionnaires was the only aspect of the research.

(b) Section 46.116(a)(5): A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. OHRP finds that the description of the coding of samples and data, handling of identifiers, and sharing of information in the informed consent document is confusing and inconsistent in places.

(6) HHS regulations at 45 CFR 46.111(a) state that, in order to approve research covered by the regulations, the IRB shall determine that certain requirements are satisfied. OHRP finds that the investigators failed to ensure that the following requirements were satisfied during the conduct of the research:

(a) 45 CFR 46.111(a)(1): Risks to subjects are minimized, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk. It was clear from multiple interviews with the research team and staff from the participating schools that the school-based personnel were inadequately trained by the research team and did not follow uniform procedures for obtaining and documenting parental permission and subject assent and for collecting subject data. Such deficiencies reflect a failure to follow procedures consistent with sound research design.

(b) 45 CFR 46.111(a)(7): When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Correspondence between the investigators and the schools as well as interviews with research team members indicated that, on at least one occasion, numerous signed informed consent documents were lost by the schools.

(7) HHS regulations at 45 CFR 46.103(a) require that each institution "engaged" in human subjects research that is conducted or supported by HHS provide OHRP with a satisfactory assurance of compliance with the regulations, unless the research is exempt under 45 CFR 46.101(b). (Please see OHRP guidance at http://ohrp.osophs.dhhs.gov/humansubjects/assurance/engage.htm)

An institution becomes "engaged" in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d),(f)].

OHRP finds that (a) all of the participating SATURN high schools were engaged in human subjects research funded by HHS and (b) none of these sites obtained an OHRP-approved assurance for this research.

OHRP Action

In view of the above determinations and in order to ensure adequate protections for human subjects, the Office for Human Research Protections hereby restricts the OHSU Assurance (FWA-161). Under this restriction, the applicability of FWA-161 to the above-referenced research project (the SATURN study) is suspended, effective immediately. Under this suspension, no new subjects may be enrolled in the SATURN study and research interventions and interactions with currently enrolled subjects in the SATURN study must be suspended.

Required Actions

(1) OHSU must develop a satisfactory corrective action plan to address all deficiencies and concerns described above as a condition for OHRP consideration of removal of the restriction on the OHSU FWA.

(2) The IRB must re-review the SATURN protocol. This review must include review of the complete grant application, and should consider the need to re-consent already- enrolled subjects. In its review, the OHSU IRB should determine that the following requirements are satisfied:

(a) Risks to subjects are minimized.

(b) 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.

(c) Selection of subjects is equitable.

(d) Informed consent will be sought from each prospective subject or the subject's legally authorized representative.

(e) Informed consent will be appropriately documented. This includes ensuring that the investigator seeks consent only under circumstances that provide the prospective subject or the subject's representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

(f) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(g) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(h) 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.

(3) OHSU should ensure that proper assurance mechanisms are put into place for the participating schools. Please contact George Gasparis, Director, Division of Assurances and Quality Improvement, OHRP at 301-402-5164 for assistance.

OHRP encourages OHSU to develop its corrective action plans expeditiously, and forward them to OHRP for review as soon as possible. OHRP is available to assist OHSU in the development and implementation of these corrective action plans. Do not hesitate to contact me should you have any questions.

Sincerely,

Kristina C. Borror, Ph.D.
Compliance Oversight Coordinator
Division of Human Subject Protections

cc: Dr. Gary T. Chiodo, OHSU IRB#1 & #3 Chair
Dr. Susan Hansen, OHSU IRB#2 Chair
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