

**DEPARTMENT OF HEALTH SERVICES**

GENETIC DISEASE BRANCH  
2151 BERKELEY WAY, ANNEX 4  
BERKELEY, CA 94704  
510/540-2534



November 19, 2001

Dear Chief Executive Officer:

The enclosed newsletter announces the initiation of a statewide research project, which should result in a better and more comprehensive screening of newborns for inherited metabolic disease. The California Healthcare Association encourages your participation and cooperation in this endeavor.

This project which involves the use of already collected blood specimens will be conducted in maternity hospitals statewide by the Department of Health Services (DHS). The exact date for initiation of the project will be announced soon and additional detailed information will be forwarded to you one month prior to the starting date.

Since this is a research project, the issue of protection of human subjects needs to be addressed. The project was reviewed and approved by the Institutional Review Board (IRB) for the state health agencies. The approval letter is included in this mailing. The State IRB has determined that the consent form meets all the requirements of 45 CFR 46.116. The consent form is a long form and as such, does not require a witness. A copy of the consent form is included. The consent form has a space for witness, but this is optional.

The hospital is only participating to the extent of obtaining the informed consent for the use of an already collected blood specimen to run an additional test, Tandem Mass Spectrometry (MS/MS). Under state law, the specimen must be collected and tested by the State for Phenylketonuria, Congenital Hypothyroidism, Hemoglobin disorders and Galactosemia. The MS/MS analysis imposes minimal risks as defined in 45 CFR 46.102 (I).

The hospital has three options under federal regulations for the protection of human subjects:

- (1) Accept the state IRB approval as acceptable in place of hospital IRB review.
- (2) Distribute the state materials, only without additional explanation.
- (3) Submit the project to the hospital IRB for formal approval.

#### OPTION I - USE OF STATE IRB

We requested the Health Resources and Services Agency to approve the use of provisions of the federal regulations that allow hospital IRBs to accept the state IRB review as meeting the federal requirements. The approval letter is enclosed. To exercise this option, the hospital needs to complete the enclosed form on hospital

letterhead, sign it, and send to the address cited in this letter. (The sample uses Kaiser as the participating hospital.) We will obtain the signature of the state IRB official and return a copy for your files.

#### OPTION 2 - DISTRIBUTION OF MATERIALS ONLY

Federal regulations 45 CFR46.103 (a) requires that each institution 'engaged' in human subject's research comply with the regulations. In guidance documents from OPRR (January 26,1999 "Engagement of Institutions in Research"), the institution would not be considered "engaged" if they decide not to obtain informed consent directly, i.e., participate personally in explaining the project or answering questions. The guidance reads:

"Institutions whose employees or agents (i) inform prospective subjects about the availability or research; (ii) provide prospective subjects with written information about research (which may include a copy of the relevant informed consent document and other IRB-approved materials), but do not obtain subjects' consent or act as authoritative representatives of the investigators; (iii) provide prospective subjects with information about contacting investigators for information or enrollment; or (iv) obtain and appropriately document prospective subjects' permission for investigators to contact them (e.g., a clinician provides patients with literature about a research study, including a copy of the informed consent document, and tells them how to contact the investigator if they want to enroll; a clinician provides investigators with contact information about potential subjects after receiving explicit permission from each potential subject)."

As you are aware, consent is more than obtaining a signature from a subject on a consent form — it is a process that involves information exchange between the subject and the investigator until the subject understands the information presented in the consent document and agrees to voluntarily participate in the study. If the printed information provided by the state investigators is sufficient in the subject's opinion to consent to participation, the hospital personnel can obtain the signature and forward the specimen with a (yes) sticker. If the mother requires additional information in order to understand the project before signing the form, she can be referred to the state investigators or choose not to participate in the project. If the hospital accepts this interpretation of their role, they would not be "engaged" in research and institutional IRB review would not be required.

This is a research project carried out by the DHS under state law. The DHS developed the research protocol, the data collection system, and informed consent form. The State will perform and interpret the analysis on samples submitted to the DHS. The hospitals are receiving no funds, state or federal for participation and are not included as investigators. Therefore, there is no hospital investigator signature required on any form by the state.

### OPTION 3 – SUBMIT PROJECT TO HOSPITAL IRB FOR FORMAL APPROVAL

Should you decide that a hospital IRB approval is required, you will need to take the following steps:

- (1) Until hospital IRB approval is obtained, your staff will have to manually remove the supplemental insert (purple pages) from the newborn screening booklet that is required to be distributed to every mother. These pages describe the project and include the informed consent form. The rest of the booklet (white pages) explains the current newborn screening done by the state. Your hospital will have to develop a policy to respond to women who request the test during the review period.
- (2) Since women will learn of the test during prenatal care and many other hospitals will be participating in offering the state supplemental screening at no charge and will be publicizing the pilot project, the hospital staff should be prepared to explain to inquiring mothers why the hospital is not permitting them to participate pending IRB review.
- (3) If the hospital IRB approves a consent form different from the state form, the mother would have to sign both forms. Until the state can obtain permission from the State IRB to accept the hospital's form as a substitute, the hospital will be responsible for printing and distributing the substitute and will be engaged in research, including obtaining informed consent, i.e., explaining and answering questions.

If the hospital decides that they will seek hospital IRB approval, they need to notify the Genetic Disease Branch (GDB) as soon as possible. GDB staff will provide materials to assist in obtaining IRB approval.

Please send this notification and request to:

California Department of Health Services  
Genetic Disease Branch  
2151 Berkeley Way, Annex 4  
Berkeley, CA 94704  
Attention: Kate Steiner or email to: [ksteiner@dhs.ca.gov](mailto:ksteiner@dhs.ca.gov)  
510-883-6772

### STATE LAW

Hospitals also are obligated to observe state law regulating human experimentation, Health and Safety Code Section 24170, etc. seq. These code provisions apply only to medical experiments as defined in Health and Safety Code 24174. The definition does not cover consent for the use of a specimen already collected as part of the person's standard health care. It covers only experiments, which require penetration or damaging

Chief Executive Officer

Page 4

November 19, 2001

of tissues, use of drug or device, biological substance or organism not related to maintaining or improving the health of the subject. In other words, it applies to experimentation that usually involves more than minimal risk to subjects. The protocol as approved by the State IRB is in compliance with state and federal law.

HIPAA

Hospitals need not be concerned with any HIPAA privacy implications, as this project will be completed before HIPAA requirements must be met by April 14, 2003.

We appreciate the burden that these changes in our newborn screening program impose on hospitals. However, we are soliciting your cooperation and support because we are certain that they will result in a worthwhile prevention of heritable metabolic disease.

If you need additional information or counsel, please feel free to contact us at the following numbers: George C. Cunningham, 510-540-2552; Lois Richardson, 916-443-7401.

Sincerely,



George C. Cunningham, M.D., M.P.H.,  
Chief  
Genetic Disease Branch



Lois Richardson, Esq.  
Legal Counsel  
California Healthcare Association

Enclosures

**cc:** Director of Perinatal Services  
Chief Nursing Officer