

**PRELIMINARY REVIEW CHECKLIST
FOR NEW PROPOSALS**

ITEM	Explanation
Date Received	December 3, 2007
IRB Project #	07-187
Protocol Title	New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study
Principal Investigator	Amy Hietala
Project Description	MDH Newborn Screening Program in collaboration with Perkin Elmer Life & Analytical Sciences (PE) is prosing to demonstrate equivalence or superiority between two assays for performance and specimen results in the determination of Galactose-1 Phosphate Uridyl Transferase (GALT) activity in neonatal diagnostic dried blood spot specimens. Galactosemia is one of the 54 disorders on Minnesota's screening panel.
Co-PI	Helena Karvonen (PerkinElmer Life & Analytical Sciences in Turku, Finland)
Review by other IRB?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No if yes who
Application Signed?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Informed Consent Included?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Not applicable
If no, has PI been contacted?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Data Practices Act listed?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable
MDH funded?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Other funding (specify)?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No PerkinElmer Life & Analytical Sciences Turku, Finland
Other concerns/issues:	

Staff comments to Primary Reviewer:

Recommended Action:

Full Board review; add to next month's agenda. Primary Reviewer: _____

Return to PI for completion

Send to _____ for expedited review

Send letter of exemption from full IRB review - *Category #4* *PR*

Send to Data Practices Coordinator



HELLO PETE! 07-155 11/27
 HERE IS AN IRB APPLICATION FOR
 ANOTHER TESTING KIT EVALUATION
 IN NEWBORN SCREENING. THIS IS
 SIMILAR TO THE STUDY WE DID
 ON TOTAL GALACTOSE EARLIER
 THIS YEAR. IF THAT HELPS.

Health
 rd

IRB Staff USE ONLY
 ID #: 07-187

Title of Research:

THANK-YOU!
 AMY HIETALA 07-177

with Human Subjects

Principal Investigator

THANK-YOU!

Name: Amy

AMY HIETALA

(phrase) Feasibility Study

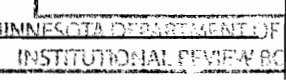
601 Robert Street N

MN 55155
 State Zip

Title: Research Scientist 2

E-Mail/Internet Address:

Phone Number: 651-201-5465



Amy.Hietala@health.state.mn.us

Fax Number: 651-201-5465

Funding Agency Information:

Address: Wallac Oy, PO Box 10, FIN-20101

Name: Helena Karvonen and/or Elina Tuomola,
 PerkinElmer Life & Analytical Sciences

Turku, Finland

Phone Number: +358 2 2678 482 and/or -887

E-Mail/Internet Address:

Fax Number: +358 2 2678 357

helena.karvonen@perkinelmer.com and/or
 elina.tuomola@perkinelmer.com

If known, Application or Proposal Identification Number:

Proposed Project Dates: From: January 2, 2008 To: February 28, 2008
 Month/Day/Year Month/Day/Year

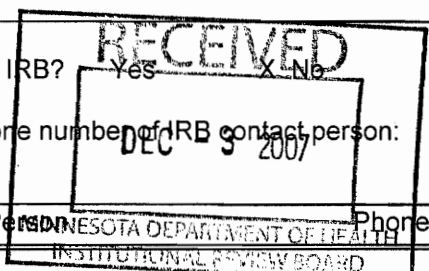
Is this project being reviewed by any other IRB? Yes No

If yes, give name and phone number of IRB and contact person:

Name _____ Phone Number _____
 Has this project been approved by another IRB? Yes No

If yes, give date of approval, name and phone number of IRB contact person: _____
 Date of Approval _____

Name of Contact Person _____ Phone Number (include Area Code) _____



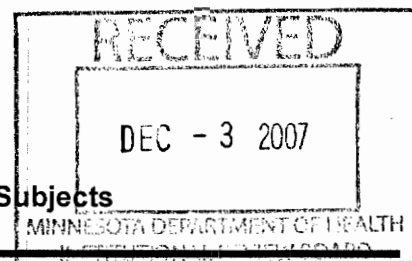
I CERTIFY THAT THE INFORMATION FURNISHED CONCERNING THE PROCEDURES TO BE TAKEN FOR THE PROTECTION OF HUMAN SUBJECTS IS CORRECT. I WILL SEEK AND OBTAIN PRIOR APPROVAL FROM THE IRB FOR ANY SUBSTANTIVE MODIFICATION IN THE PROPOSAL. I WILL PROMPTLY REPORT TO THE IRB ANY UNEXPECTED OR SIGNIFICANT ADVERSE EFFECTS (E.G., BREACHES OF CONFIDENTIALITY, BREACHES OF PROTOCOL, WITHDRAWAL OF STUDY SUBJECTS, AND COMPLAINTS ABOUT THE STUDY) IN THE COURSE OF THIS STUDY.

Signature of Principal Investigator *Amy Hietala*

Date 11-27-2007

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I. PURPOSE OF THE STUDY, INCLUDING THE RESEARCH QUESTION (S).

The Minnesota Department of Health Newborn Screening Program in collaboration with Perkin Elmer Life & Analytical Sciences (PE) is proposing to demonstrate equivalence or superiority between two assays for performance and specimen results in the determination of galactose-1-phosphate uridyl transferase (GALT) activity in neonatal diagnostic dried blood spot specimens. Equivalence or superiority will be determined between the current Neonatal GALT (NG-1100/NG-4100) assay and a new GALT assay using the Victor 3™ fluorometer and 1000 de-identified dried blood spot specimens. Deficiency or low activity of the GALT enzyme results in the metabolic disorder, galactosemia. Galactosemia is one of the 54 disorders on Minnesota's screening panel.

Research questions addressed by this study are:

- Is the new GALT kit design significantly better than the current Neonatal GALT (NG-100/NG-4100) kit? Does the new GALT kit demonstrate better stability than the current GALT kit?
- Is the new GALT kit protocol easy enough to perform?
- What are the cut-off values for normal/abnormal GALT levels as determined by the new GALT kit and how does this compare to the current cut-off values?
- Do the calibration standards cover the clinically relevant range and is the precision of the kit acceptable?
- What is the patient median and distribution for the GALT enzyme in Minnesota's newborn population as determined by assaying a minimum of 1000 de-identified residual neonatal dried blood spot specimens with the current and new GALT kits?

De-identified results will be reported back to PE for evaluation analysis, where they are reported as part of a feasibility study for the new GALT kit. Results may be included in the kit insert and may be used to obtain regulatory approvals. The results will be reported as part of the PE design history file for this product. The results obtained with the evaluation kit will NOT be used for reporting clinical results.

If the new GALT kit proves to be more stable than our current GALT kit, a change over to the new product is anticipated. Results may also be used as part of the Minnesota laboratory's verification of the new GALT kit in the event that we use this as an alternative method for measuring the activity of the GALT enzyme.

II. RESEARCH METHODS - Include the following:

A. Description of the subject population - number of subjects, age range, how subjects will be identified and selected;

Specimens that are routinely analyzed for GALT activity with our current GALT assay will be analyzed again for GALT activity with the new kit until 1000 acceptable values have been generated. Specimens are de-identified and associated only with the MDH accession number. Satisfactory specimens are defined as specimens greater than 24 hours of age where the dried blood spot quality is acceptable (not layered, scratched or insufficient quantity).

The age range will be the newborn period from greater than 24 hours of age to less than 7 days of age.

In addition, a minimum of 5 low GALT activity specimens representing positive galactosemia infants will be retrieved from storage, de-identified, and analyzed for GALT activity with the current GALT assay and the new GALT assay.

The newborn screening laboratory routinely de-identifies specimens and uses them for research on the prevalence of disease and other health conditions. It has also been standard operating procedure to use de-identified specimens when verifying a new test assay or determining normal and abnormal test result ranges.

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Federal regulations [45 CFR 46.100(b)(4)] do not require IRB review of "research involving the collection, study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects."

B. Explanation of subject involvement in the research (the who, what, when, and how of subject involvement);

Subject involvement is non-existent. Dried blood spot specimens from Minnesota's newborns are routinely screened for 54 disorders by the MDH newborn screening program as mandated by law. This study will simply take one additional punch from the dried blood spot we already have and analyze it for GALT activity using the new Perkin Elmer Life & Analytical Science's GALT kit. Only the MDH accession number, specimen sampling date, analysis dates, and GALT activity results from both kits will be shared with PE. Absolutely no demographic information will be reported.

Precedence in the Minnesota Department of Health Public Health Laboratory has been that residual diagnostic specimens may be used without permission for research purposes if the subject is not identified. The Newborn Screening Program is continuously developing and validating new tests for treatable conditions. Anonymous newborn blood spots are used to be sure that new tests are accurate and determine the ranges of normal and abnormal values. Parents that have opted out of storage of the dried blood spot and/or test results for their child will not have their child's dried blood spot specimen included in this study.

C. Summary of data analysis or statistical methods to be used in the study;

The data collected will be the GALT activity of the dried blood spot specimen as determined by the current kit and the new kit. Data will be in units/gram hemoglobin (U/gHb) or Units per volume of blood (U/dL), respectively. Data analysis will consist of evaluating whether or not low GALT activity specimens were identified as such by both assays and the normal specimens were identified correctly by both assays. The statistics used to determine the normal/abnormal range and cut-offs will consist of patient median values, lower percentiles (0.5th, 1st, 1.5th, 2nd, 5th, etc.), standard deviations of the normal population, and other appropriate descriptive statistics as determined by each assay.

In addition, quality control specimens provided by the kit vendors and the CDC's Newborn Screening and Quality Assurance Program (NSQAP) will be evaluated to ensure they are within two standard deviations of the mean. Duplicate values of the calibration standards and quality control specimens will be evaluated by the percent coefficient of variation. Lastly, the correlation coefficients of the calibration curves will be evaluated, and the curves fitted by including calibrator A (no GALT activity) as a first calibration point or by using it as a background level or blank. This assures that the specimen data is of good quality.

D. Specification of any inducements or rewards to be given subjects for their participation;

Not Applicable. Inducements or rewards are not given for participation in newborn screening.

E. Specification of any research-related expenses to be charged to the subject or their third party payer.

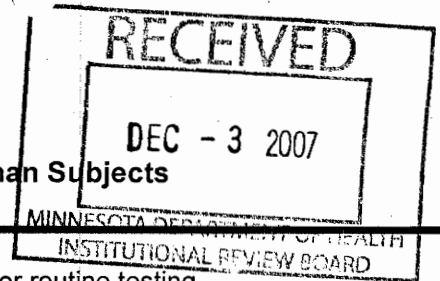
Not Applicable. This study uses residual diagnostic dried blood spot specimens.

III. **RISKS** Describe any reasonably foreseeable risks or discomforts to participants, including physical, emotional, economic, or social factors. Delineate any steps taken to minimize risks, as well as care of subjects in the event of an accident or complication.

Not Applicable. There are no foreseeable risks or discomforts to participants. The MDH screening laboratory

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already has the residual diagnostic dried blood spot specimens on site for routine testing.

IV. BENEFITS Describe all reasonably foreseeable direct benefits to subjects as well as potential benefits to society.

The benefit would not be translated directly to the subjects tested in this study. The benefit is that the MDH newborn screening laboratory may have an improved and more stable assay for GALT activity. The screening laboratory is high throughput and we keep a large inventory of kits to fulfill our objective of screening all newborns. It is crucial that these kits are stable enough to allow for long term storage. In addition, the GALT assay is our primary screen for galactosemia, which is one of the most acute metabolic disorders on the screening panel.

V. CONFIDENTIALITY AND PRIVACY OF DATA Include the following:

A. An explanation of the procedures that will be implemented to safeguard data privacy, including how and where the data will be stored, in what form the data will be stored, how long the data will be stored, methods for destroying the data, and how the anonymity of the subject will be insured. The classification of the data under the Minnesota Government Data Practices Act or other relevant statutes should also be submitted, as well as specific security measure to be used.

Data privacy will be maintained and the anonymity of the subject insured by not associating demographic data with the specimen GALT activity or the MDH accession number. The data consisting only of de-identified MDH accession numbers, sampling date, analysis date, and numeric results (electronic and paper) will follow our current records retention schedule of four years plus the current year, and then be deleted from the system. The residual diagnostic dried blood spot specimens are stored indefinitely in a locked freezer accessible by newborn screening personnel trained in the MDH Public Health Laboratory's Data Practices. De-identified data that is transferred from the Principal Investigator to PE will be behind the MDH firewall and all personal computers used for the analysis of the data are password protected.

The residual diagnostic dried blood spot specimens with demographic data and the analytical data are classified as private under MN Statute 13.3805.

B. Identification of all persons who will have contact with private information, including research staff, clerical staff, network administrators, and computer staff. Describe how these persons will maintain confidentiality of the data.

The only people in contact with the data generated from this feasibility study will be the principal investigator, newborn screening staff, and PE personnel working on this study. Newborn screening staff is responsible for maintaining the confidentiality of the data under newborn screening program standard operating procedures. Only de-identified data will be reported to PE personnel working on this study.

VI. INFORMED CONSENT

Attach a copy of the proposed consent form. Please describe procedures for obtaining consent.

NOTE: You must submit a consent form or letter that contains all of the elements of informed consent as outlined in the Informed Consent Checklist on page 5 of this application.

Not Applicable

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VII. RESEARCH INSTRUMENTS

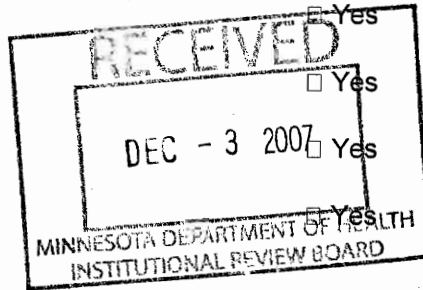
Attach copies of all instruments to be used (questionnaires, surveys, etc.)

Attachments include: New GALT Feasibility Study: Characterization of the Feasibility of a New Neonatal GALT assay using routine specimens from the state of Minnesota NBS Program; and Appendix 1-Assay Procedure (New GALT Feasibility Study, Study number 07020).

VIII. VULNERABLE POPULATIONS CHECKLIST

Will your research involve any of the following? If yes, attach a list of additional safeguards you will use.

- | | | |
|---|------------------------------|-----------------------------|
| A. Prisoners? | <input type="checkbox"/> Yes | X No |
| B. Pregnant Women? | <input type="checkbox"/> Yes | X No |
| C. Children? | X Yes | <input type="checkbox"/> No |
| D. Cognitively Impaired Persons? | <input type="checkbox"/> Yes | X No |
| E. Economically or Educationally Disadvantaged Persons? | <input type="checkbox"/> Yes | X No |
| F. Fetuses? | <input type="checkbox"/> Yes | X No |
| G. Human In-Vitro Fertilization? | <input type="checkbox"/> Yes | X No |
| H. HIV Antibody Testing? | <input type="checkbox"/> Yes | X No |
| I. Non-English Speaking Participants? | <input type="checkbox"/> Yes | X No |



Additional Safeguards:

No additional safeguards are necessary. This research does not add any additional risk to the already established risks and benefits of Minnesota's mandated blood spot newborn screening program.

Attached additional sheets if necessary.

Since these subjects, and others like them, who are either not competent or not free to give their own consent, are particularly vulnerable to coercion and undue influence, investigators must incorporate safeguards in the research plan, and be certain to document fully their informed consent or the informed consent of their legal representatives.

PLEASE BE SURE TO SIGN PAGE 2 OF THIS APPLICATION

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Informed Consent Checklist

/	<i>Elements</i>
	A statement that the study involves research.
	An explanation of the purposes of the research.
	The expected duration of the subject's participation.
	A description of the procedures to be followed.
	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 which may reasonably be expected from the research.
	A disclosure of appropriate alternative procedures or courses of treatment, if any, that might 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 an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained.
() Research Qs	An explanation of whom to contact for answers to pertinent questions about the research (research study contact name and phone number) and research subjects' rights (IRB contact name and phone number, e.g., Cindy Turnure, Ph.D. 651-296-6351), and whom to contact in the event of a research-related injury to the subject.
() Rights Qs	
() Injury Qs	
	A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled.

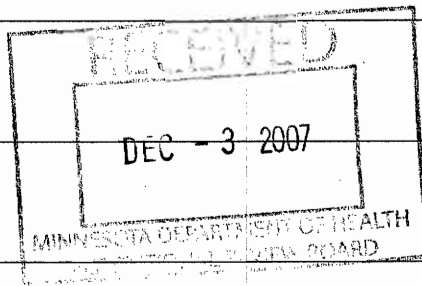
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Application for Approval of Research with Human Subjects

HIPAA Checklist

Y YES	Y NO	Elements
	No	<p>1. Will any of the information for the study be "protected health information" (PHI) that the study obtains directly from a HIPAA "covered entity"? (Exact definitions of "covered entity" and "PHI" are available at www.hhs.gov/hipaa. For the most part, however, you can use the following definition):</p> <ul style="list-style-type: none"> • A HIPAA "covered entity" includes providers (hospitals, clinics, doctors, etc.), health plans (health insurers, HMOs), and health care clearinghouses (go-betweens for providers & plans). NOTE: MDH is not a covered entity under HIPAA and any health information that MDH has collected or received for public health purposes is not PHI in MDH's possession. • PHI is individually identifiable health information that is held by a covered entity and that relates to the health condition of an individual, the provision of health care to an individual or the payment for the provision of health care. <p><i>If you answered no to this question you do not have to complete the rest of the checklist.</i></p>
		<p>2. Has the research been reviewed by a Privacy Board or another IRB for HIPAA purposes? If yes, specify which entity is doing this review and submit their review when available.</p> <p>_____</p>
		<p>If no, are you requesting this IRB to review HIPAA requirements? If yes, you will be contacted by MDH staff for further information.</p>





Study Number 07020

New GALT Feasibility Study: Characterization of the Feasibility of a New Neonatal GALT assay using routine specimens from the State of Minnesota NBS Program

Sponsor PerkinElmer Life and Analytical Sciences
Wallac Oy
P.O.Box 10, FIN-20101 Turku
Finland

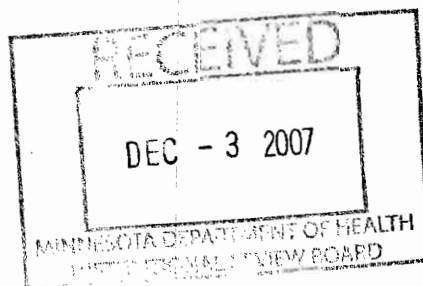
Study site Minnesota Department of Health
PO Box 64899
St. Paul, MN 55164-0899

Management of the study:

Principal Investigator::	Amy Hietala
Project Manager, PerkinElmer Life and Analytical Sciences, Wallac Oy:	Elina Tuomola, Ph.D.
Product Manager, PerkinElmer Life and Analytical Sciences, Wallac Oy:	Helena Karvonen

NOTE: Information contained in this protocol is confidential and should not be disclosed without written consent from the sponsor or its representative.

FOR FEASIBILITY USE ONLY.



1 SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to stipulated local legal and regulatory requirements.

Principal Investigator (Researcher):

Signed: _____
Amy Hietala

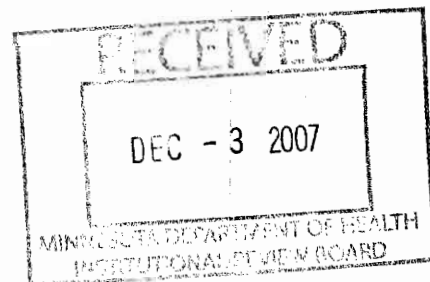
_____ Date

PerkinElmer Life and Analytical Sciences, Wallac Oy:

Project Manager:

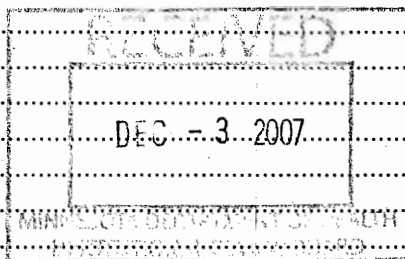
Signed: _____
Elina Tuomola, Ph.D.

_____ Date



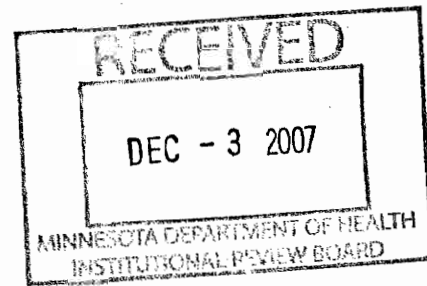
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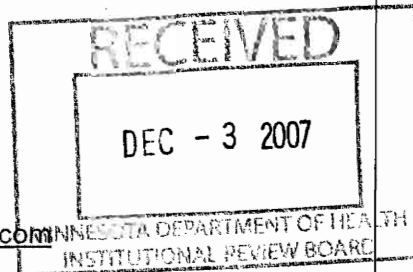
3 LIST OF ABBREVIATIONS AND TERMINOLOGY

CFR	Code of Federal Regulations
DBS	Dried blood spot specimen
FDA	Food and Drug Administration
IDE	Investigational Device Exemption
IEC	Independent or Institutional Ethics Committee
IRB	Institutional Review Board
PKI	PerkinElmer Incorporation
SOP	Standard Operating Procedure



4 STUDY MANAGEMENT

<p>Study site: Minnesota Department of Health 601 Robert Street North St. Paul, MN 55155-2531</p>	<p>Study site investigator: Amy Hietala Phone: 651-201-5455 Fax: 651-201-5465 E-mail: Amy.Hietala@state.mn.us Mailing Address: PO Box 64899 St. Paul, MN 55164-0899</p>
<p>Sponsor: PerkinElmer Life and Analytical Sciences, Wallac Oy, P.O.Box 10, FIN-20101 Turku, Finland Fax: +358-2-2678 357</p>	<p>Product Manager/Contact Person: Helena Karvonen Office : +358-2-2678-482 Mobile : +358-40-744 6172 Email: helena.karvonen@perkinelmer.com</p> <p>Project Manager : Elina Tuomola, Ph.D. Office : +358-2-2678-887 Mobile : +358-40-766 9202 Email: elina.tuomola@perkinelmer.com</p>
<p>Local support PerkinElmer Life and Analytical Sciences</p>	<p>Janet Perkins Genetic Screening - Sales 710 Bridgeport Ave. Shelton, CT 06484-4794 phone: 330-242-5312 fax: 203-944-4901 E-mail: janet.perkins@perkinelmer.com</p>



5 PROTOCOL SUMMARY

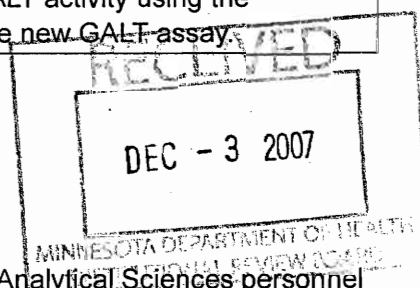
Title:	New GALT Feasibility Study: Evaluation of the Feasibility of a New Neonatal GALT assay using routine specimens from the State of Minnesota NBS Program
OBJECTIVES:	
	<p>The objective of this study is to provide information on the feasibility of a new GALT assay in comparison with the present GALT screening assay.</p> <p>The study will be performed using anonymized specimens provided by the Minnesota newborn screening program.</p>
Study Duration:	3-4 weeks from the initiation of the study.
Specimen:	The study specimens are routine newborn screening DBS that are collected and stored independently of this study. The study will include at least 1000 specimens analyzed for GALT activity using the Neonatal GALT NG-1100/4100 kit and the new GALT assay.

6 BACKGROUND

This document is intended to be read only by PerkinElmer Life and Analytical Sciences personnel and the study group at the evaluation laboratory.

The purpose of this document is to describe the protocol for the feasibility study of a new Neonatal GALT under development, hereafter New GALT. This kit is intended for the semiquantitative determination of enzymatic activity of galactose-1-phosphate uridylyl transferase (GALT) in blood specimens dried on filter paper. The reagents used in the feasibility study are for the study.

Deficiency of GALT enzyme results in a form of the inherited metabolic disorder, classic galactosemia. Galactosemic patients can not metabolise galactose leading to accumulation of



galactose and galactose-1-phosphate. Classical galactosemia leads to severe symptoms within few weeks after birth if not recognised and treated by elimination of lactose and galactose in the diet. Therefore, screening of GALT activity is included in many NBS programs.

The GALT screening is not a diagnostic test. Galactosemia can only be determined by a diagnostic test.

7 STUDY OBJECTIVES

The primary objective of this study is to provide information on the GALT test kit in comparison to the NG-1100 Neonatal GALT kit. The new design differs from the current kit version as

- Calibration points have been modified
- Calibrators on cassette instead of sheet
- Unit definition has been changed from unit/g hb to unit/volume blood
- Kit controls on cassette
- Normal control of human origin
- One vial of substrate reagent per 4 plates
- Clear plate
- Assay buffer composition changed, a new bottle

In addition, the assay protocol has been changed

- A pretreatment step has been added
- Shaking instead of tapping the plate
- Incubation time shortened from 3 h (\pm 30 min) to 2 h
- Ethanol replaced with assay buffer as stopping reagent (haemoglobin is not longer precipitated)
- No settling time required

Finally, measuring time has been changed from 0.2 seconds to 1 second.

Performance characteristics of the new design have not been established yet. Therefore, results from the feasibility study using the New GALT in its intended use will be important in order to receive customer feedback. The most important questions to be answered include

- Is the new design significantly better than the current kit?
- Do the calibrator points cover the clinically relevant range?
- Is the distribution of normal samples acceptable in order to separate presumptive positive and negative samples?
- Is the activity of the normal control close to the median of the samples?
- Is the precision acceptable?
- Is the assay protocol easy enough to perform?
- Do the punched disks float in the well at the time of measurement?



Additionally, Time Resolved Fluorescence measurement should be performed on each plate in order to collect information about the signal level for further purposes.

The results should be reported back to PerkinElmer (PKI) for feasibility analysis. The results and the customer feedback are used to evaluate whether the performance of the redesigned assay meets the clinical requirements and criteria set by the end user of the product. The results will be reported as part the PKI design history file of the product. The results obtained with the New GALT under development must not be used for reporting clinical results.

8 STUDY SPECIMENS

The study specimens are routine newborn screening specimens that are collected and stored independently of this study. The specimens used in the study must meet the specimen quality criteria of the State of Minnesota NBS program.

Accession number will be used during specimen laboratory analysis and that number will be linked to the original GALT screening result. Patient identification information must not be revealed or included in the study data. The study site investigator is responsible for setting up systematic coding records to connect the study results to the screening data without patient identification.

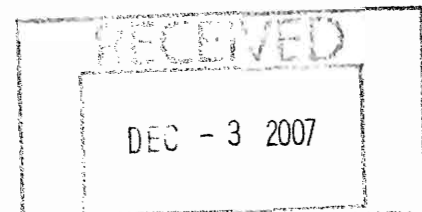
Information about sample date (when taken), date analysed using Neonatal GALT kit NG-1100/4-100 and analyzed using the New GALT assay is required as GALT activity may decrease during storage.

9 STUDY PRODUCT

9.1 Intended Use

The New Neonatal GALT assay under development is intended for the semiquantitative determination of galactose-1-phosphate uridyl transferase (GALT) activity in blood specimens dried on filter paper.

The kit is used for feasibility study use only. The performance characteristics has not been established. Not for use in diagnostic procedures.



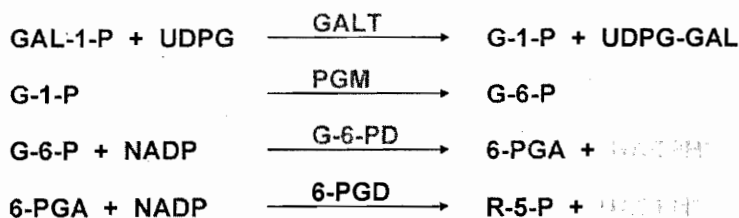
9.2 Study Product Description

9.2.1 Acquisition

The product is manufactured by PerkinElmer Life and Analytical Sciences, Wallac Oy, Mustionkatu 6, Turku, Finland.

9.2.2 Neonatal GALT Assay Principle

Determination of GALT activity is based on the coupled enzyme reaction described below (1). The reaction flow is the same as in kit NCS Neonatal GALT NG-1100/4100.



*Fluorescent product to be measured.



In brief, galactose-1-phosphate (GAL-1-P) and uridine 5'-diphosphoglucose (UDPG) are substrates for the GALT enzyme in the first reaction. Glucose-1-phosphate (G-1-P) produced by GALT is further converted into glucose-6-phosphate (G-6-P) by the enzyme phosphoglucomutase (PGM). In the following reaction, G-6-P is converted into 6-phosphogluconate (6-PGA) by the enzyme glucose-6-phosphate dehydrogenase (G6PD) in a reaction involving reduction of nicotinamide adenine dinucleotide phosphate (NADP) into a fluorescent nicotinamide adenine dinucleotide phosphate, reduced (NADPH). In addition, 6-PGA (6-phosphogluconate) is converted into R-5-P (ribulose-5'-phosphate) by 6-PGD (6-phosphogluconate dehydrogenase) in a reaction also reducing NADP into fluorescent NADPH.

The fluorescence can be measured using excitation central wavelength of 355 nm and emission central wavelength of 460 nm. If GALT is deficient in the specimen the fluorescent end product is not formed during the assay and the screening result should be considered as presumptive positive.

9.2.3 Product Storage and Stability

The New GALT reagents should be stored at +2 to +8°C and the calibrators and controls at -20°C until the expiry date informed by PKI. Instructions for handling the opened reagents are given in a separate Assay Procedure (Appendix 1).

9.2.4 Labeling

The study reagents are for this feasibility study only. The performance characteristics of this product have not been established. The reagents are labeled based on the manufacturing day, not the expiry date.

9.2.5 Warnings and Precautions

See the Assay Procedure (Appendix 1) for details on warnings and precautions.

9.3 Materials and Method

9.3.1 Materials

PerkinElmer provides all the necessary Neonatal GALT reagents that are needed for completion of the feasibility study.

9.4 Methods

Calibration

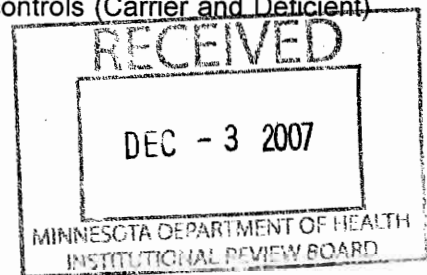
The calibrators have numbers from 1 to 6 (in the final kit from A to F). The GALT activities are given in the New GALT specific document. A calibration curve in duplicate should be run on each plate.

Controls

The new GALT includes two controls: normal and abnormal. These controls should be run on each plate in duplicate. Preliminary mean values are provided by PerkinElmer. A site specific mean value and acceptance limits for controls should be established. Each run is accepted based on control values. Rejected data should be documented and delivered to PerkinElmer with any discovered acceptable causes and problems. In addition to kit controls two controls (Carrier and Deficient) provided by PerkinElmer should be run on each plate in duplicate.

Assay procedure

The assay procedure is described in Appendix 1.



10 STUDY DESIGN

The purpose of this study is to collect information about the performance of the new GALT design and to receive customer feedback concerning the assay protocol. The performance of the new GALT will be compared with the current method Neonatal GALT kit NG-1100/4100. The goal is to collect data from at least 1000 specimens in order to

- study assay precision (CV%) based on the controls obtained by PerkinElmer

- evaluate distribution of the normal population
- calculate different lower percentiles for preliminary cut-off values using the new assay
- estimate the number of floating discs

The study site should have a signed copy of the protocol upon commencement of the study. The feasibility study certification (Appendix 2) should be signed before the study begins. The signed documents should be returned to the project manager before the feasibility study begins.

10.1 Training and familiarization period

Handling of reagents and the detailed assay protocol are described in the Assay Procedure (Appendix 1).

During the training period the study site personnel will be trained to perform the new GALT by PerkinElmer Product Chemist visiting the study site (Ville Väisänen, Ph.D). The study site personnel will run at least five new GALT assays including a calibration curve in duplicate and the two controls (Normal and Abnormal) each with 10 replicates. Assays should be performed according to the Assay Procedure. The mean value and SD for both controls are calculated.

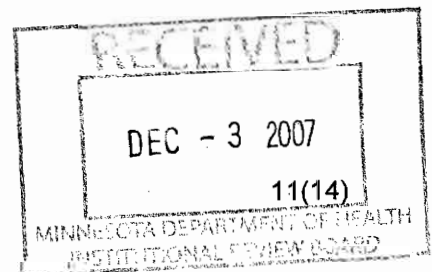
The preliminary targets for the controls are stated in a New GALT specific document. MultiCalc files of all the runs of the training will be evaluated by the Product Chemist visiting the study site. New site specific targets (=mean) and acceptance limits ($\pm 2SD$) for the controls are calculated by the Product Chemist. The site specific targets should be within $\pm 2SD$ of the preliminary target values. Laboratory specific limits have to be calculated and accepted before start of the feasibility study phase.

10.2 Feasibility Study

At least 1000 samples should be measured using the Neonatal GALT kit NG-1100/4100 and the new GALT. A calibration curve in duplicate should be run on each plate using six calibrators. Also the controls (abnormal and normal levels) should be run in duplicate on each plate.

For the study all specimens should be anonymized and randomized, and should be assayed as singlicates in the new GALT and Neonatal GALT NG-4100 assays.

The GALT activity distribution of the study population will be plotted with both methods. A number of different lower percentiles (e.g. 95th, 97th, 99th percentiles) and other appropriate descriptive statistics of results will also be reported. The distribution will be calculated using different curve fitting methods. Additionally, the curves will be fitted by including CalA (GALT activity 0 U/dL) as a first calibrator point or by using it as a background level or blank.



The assay reproducibility (CV%) is evaluated using controls Carrier and Deficient. Controls used for the imprecision study are provided with the new GALT. They should be included on each plate, once after the standards and kit controls and once at the end of the plate.

Please note! Kit controls are included in each run and the run is accepted based on control values.

10.3 Usability

The usability of the new GALT is assessed by filling a questionnaire (Appendix 3).

11 PROTOCOL AMENDMENTS AND DEVIATIONS

Changes to this study plan can only be made after discussion with the Sponsor. The changes have to be documented, signed and dated by the Study Site Investigator. All such amendments should be sent to the IRB for approval and all IRB-approved amendments will be provided to the investigator and sponsor. The investigator is responsible for submitting the protocol amendment to the IRB for approval. The protocol changes can be implemented only after a written approval has been received from the IRB.

12 DATA COLLECTION AND STUDY REPORT

Patient identification information must not be revealed or included in the study data. The data for the assay will be saved and sent via e-mail to Project Manager. Preferably, the data should be distributed to Project Manager as the study progresses.

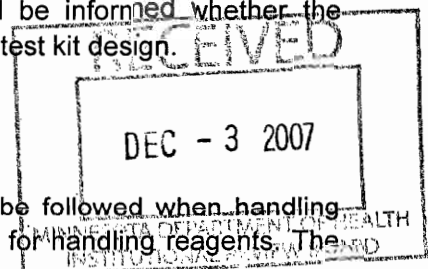
Multicalc print-outs including, raw data files containing the TRF-measurement counts and Questionnaire (Appendix 3) shall be sent to the Project manager via e-mail. Study results should be available within 4 weeks from the start of the study

All specimens collected and used in this study must be traceable to the essential information. Samples should be saved until the feasibility study is finished.

After the feasibility study is finished the primary investigator will be informed whether the developmental work will or will not be continued based on the GALT test kit design.

13 SAFETY

Standard precautions for handling biohazardous materials should be followed when handling calibrators and controls. Personnel should be aware of precautions for handling reagents. The



section "Warning and precautions" in the separate assay Procedure (Appendix 1) and the kit insert of the reference method Neonatal GALT NG-1100/4100 provides the information concerning the kit under feasibility study as well.

PerkinElmer New GALT is for feasibility study use only and must not be used for diagnostic or clinical procedures involving humans! Components are labelled with For Feasibility Use Only. Not for use in diagnostic procedures').

14 STUDY MONITORING AND SOURCE DOCUMENTS

14.1 Site Monitoring plan

Study site monitoring can be conducted to ensure that the human subject protection, study procedures, laboratory administration, and data collection processes are of high quality and meet PerkinElmer's requirements and regulatory guidelines.

14.2 Source Documents

Each participating site will maintain appropriate and required documentation for this feasibility study, in compliance with regulatory and institutional requirements for the protection of confidentiality of subjects.

15 QUALITY CONTROL AND QUALITY ASSURANCE

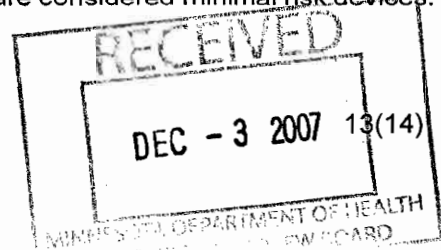
Each site should have standard operating procedures (SOPs) for quality management which describes:

- How data will be evaluated for compliance with the protocol and for accuracy in relation to source documents
- The documents to be reviewed, who is responsible, and the frequency for reviews should be identified, either in a formal quality management plan or in the study site SOPs
- The methods used for training staff should be specified

16 ETHICAL CONSIDERATIONS

16.1 Ethical Standard

The study should be carried out in accordance with the Protection of Human Subjects regulation (United States Food and Drug Administration, Title 21 CFR Part 50) and the Institutional Review Board Regulations (IRB) (United States Food and Drug Administration, Title 21 CFR Part 56), including waiver of the requirement for Informed Consent. The study is exempt from the requirement for Informed Consent and from the Investigational Device Exemption (IDE) regulations (21 CFR Part 812) because the investigational devices used are considered minimal risk devices.



16.2 Institutional Review Board

Due to regulatory requirements the participating institution should provide this protocol to an appropriate independent ethics committee (IEC) or institutional review board (IRB) for review and approval. Changes to this study plan can only be made after discussion with the Sponsor. The IRB at each site will serve as the subjects' advocates in terms of the right to privacy (i.e. in reviewing medical records). The investigators may request expedited approval from their IRBs. The study site should provide either a copy of the IRB approval or the waiver of the IRB approval to PerkinElmer, prior to initiating the study.

16.3 Confidentiality

All samples will be given a NON-PATIENT IDENTIFYING sample ID number. Patient identity, other than sample number, will not be disclosed to PerkinElmer; neither will it be included in the data set released to PerkinElmer. PerkinElmer agrees not to show the results to any third party (with the exception of regulatory authorities, e.g. FDA, EU notified bodies) without first obtaining permission of the Study Site Investigator. Results may be included in the kit insert.

Results are documented as a part of design history file of the product under development.

The Study Site Investigator will be asked to keep results confidential, unless required by law to release the results to a third party. In all other cases permission to disclose results to a third party should be obtained from PerkinElmer.

The study monitor or other authorized representatives of the sponsor may inspect all documents and records required to be maintained by the investigator.

17 REFERENCES

1. Beutler, E. and Beluda, M.C. (1965) A simple spot screening test for galactosemia. *J. Lab. Clin. Med.* **68**, 137-141

18 APPENDIXES

1. Assay procedure for the GALT test kit
2. Feasibility Use Only Certification.
This certificate should be signed by the Study Site Investigator and sent back to PerkinElmer prior to starting the feasibility study.
3. Questionnaire
4. Material Safety Data Sheet

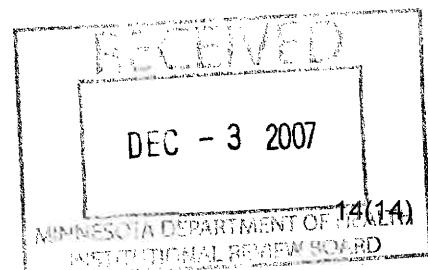
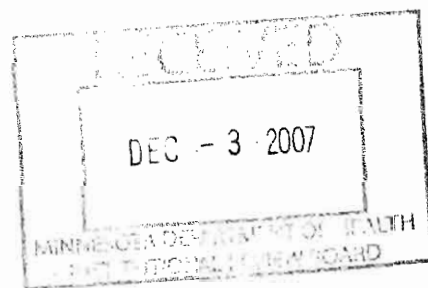


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VICTOR AND MULTICALC PROTOCOLS

Copies are to be made of the MultiCalc and Victor GALT protocols. For detailed instructions on editing parameters please see the MultiCalc and Victor D manuals.

The instructions given below assume basic familiarity with MultiCalc and Victor.

MULTICALC PROTOCOLS

Make a copy of the MultiCalc protocol "88 GALTS" or "89 GALT".

- Select F4 – Protocols
- Select F5 – Copy
- Choose the Protocol be copied ("88 GALTS" or "89 GALT")
- Name the new Program "GALTFEAS"
- Accept the protocol identifier suggested by MultiCalc or choose another identifier known to be available (must be 0-99)
- Select Measuring Technology F3 – Fluoro
- Select F2 – IFMA

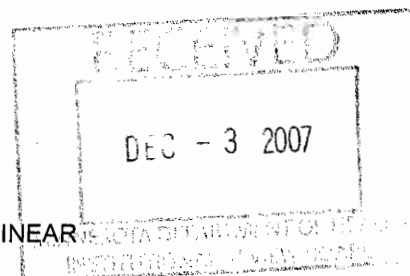
Change the replicate numbers and calibrator concentrations in the protocol.

- Select F4 – Protocols
- Select F1 – Edit
- Select Protocol "GALTFEAS"

	ASSAY TYPE IS IFMA	=	NO
01	DUAL ASSAY	=	Eu
03	MEASURING PARAMETERS	=	LIN
20	X-AXIS (CONCENTRATION)	=	MEAS
21	Y-AXIS (RESPONSE)	=	REGR UNWEIGHT LINEAR
22	FITTING ALGORITHM	=	NEW
25	STANDARD CURVE	=	NEW
26	STANDARDS ON 2.. PLATES	=	NEW

CODING

2 STD	=	A	(Make sure that the GALT calibrator concentrations correspond to those given on the lot specific quality control certificate. If this is not the case, enter the new concentrations.)
2 STD	=	B	
2 STD	=	C	
2 STD	=	D	
2 STD	=	E	
2 STD	=	F	
2 UNKN			
END			



- Select F9 – Back
- Select F1 – Quit & Save

VICTOR PROTOCOL

Make a copy of the Victor D GALT protocol.

- Open Wallac 1420 Manager
- Open Wallac 1420 Explorer
- Select protocol "GALTS" or "GALT" from Protocols/Kits panel "Neonatal USA" or "Neonatal Europe"
- Edit → Copy
- Select the folder where the new protocol is to be saved
- Edit → Paste
- Rename the protocol "GALT Feasibility"

Change the "GALT Feasibility" protocol and link it to MultiCalc "GALTFEAS"

- Open Wallac 1420 Manager
- Open Wallac 1420 Explorer
- Select protocol "GALT Feasibility"
- Open Protocol Editor by double-clicking the protocol
- Select the ID Tab
- Enter the ID number of the MultiCalc protocol "GALTFEAS"
- Select the Measurement Tab
- Double-click on the Label Operation
- Select Properties
- Change the Counting time to 1 (seconds)
- Click OK
- Click OK
- Choose Edit → Save
- Close the Protocol Editor



ASSAY PROCEDURE

Perform each determination in duplicate for both calibrators and controls. A calibration curve should be run for each plate. The unknowns can be run as single determinations. All reagents and samples must be brought to room temperature (+20-+25°C) before use.

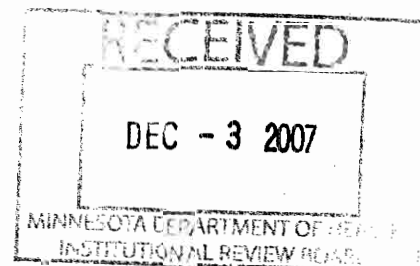
1. Preparation of reagents	Reconstituted stability *
GALT Substrate Reagent	12 hours at +20-+25°C 36 hours at +2-+8°C
GALT Substrate in Assay Buffer	6 hours at +20-+25°C 24 hours at +2-+8°C

* The stability of reconstituted reagents has not been established. The given times are minimum values to be used only in the Feasibility Study. This information should not be used for estimating the functionality of the New GALT Assay.

Reconstitute the GALT Substrate Reagent by adding 2.8 mL of deionized water to one vial. Close the vial and mix gently. One vial contains enough substrate reagent for four plates.

The GALT Substrate in Assay Buffer is prepared by adding 5 µl of GALT Substrate Reagent to 75 µl of GALT Assay Buffer. Prepare the amount of GALT Substrate in Assay Buffer needed according to the table below:

	Substrate	Assay Buffer	Total Volume
1 well	5 µl	75 µl	80 µl
1 strip	80 µl	1200 µl	1280 µl
1 plate	700 µl	10.5 mL	11.2 mL
2 plates	1400 µl	21 mL	22.4 mL
3 plates	2100 µl	31.5 mL	33.6 mL
4 plates	2800 µl	42 mL	44.8 mL

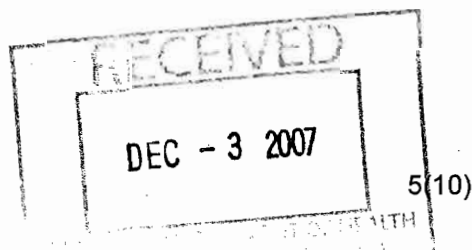


NOTE: The GALT Substrate in Assay Buffer should be prepared at least 5 minutes before use.

2. Punch out filter paper disks into the wells of a clear microplate using an automatic or a manual puncher. The diameter of the disk should be approximately 3.2 mm (1/8 inch). Include calibrators and controls in duplicate on each plate. The following plate map is given as an example. Each laboratory can decide on the best positioning of the controls and samples.

Strip	1	2	3	4	5	6	7	8	9	10	11	12
A	Cal A	Cal A	Cal B	Cal B	Cal C	Cal C	Cal D	Cal D	Cal E	Cal E	Cal F	Cal F
B	Ctrl I	Ctrl I	Ctrl II	Ctrl II	Carr	Carr	Def	Def	1 st Unk	1 st Unk	1 st Unk	etc.
C etc.												

3. Add 25 µl of GALT Assay Buffer to each well containing a filter paper disk.
4. Mix the contents of the wells for 30 seconds using a Plate Shaker and slow shaking.
5. Incubate at room temperature (+20-+25°C) for 10 minutes ± 2 minutes without shaking.
6. Add 80 µl of GALT Substrate in Assay Buffer to each well containing a filter paper disk.
7. Mix the contents of the wells for 30 seconds using a Plate Shaker and slow shaking.
8. Incubate at +37°C (+35-+39°C) for 2 hours ± 10 minutes without shaking.
9. Add 100 µl of GALT Assay Buffer to each well containing a filter paper disk.
10. Mix the contents of the wells for 2 minutes using a Plate Shaker and slow shaking.
11. Measure the time-resolved fluorescence in the Victor™ D fluorometer. Start the measurement from the Start Wizard, select "europium" and define the number of plates and samples.
12. Measure the fluorescence in the Victor™ D fluorometer. Start the measurement from the Start Wizard, select "GALT Feasibility" and define the number of plates and samples.



PROCEDURAL NOTES

1. A thorough understanding of this assay procedure is necessary for successful use of the neonatal test kit. The reagents supplied for this feasibility study are intended for use as an integral unit. Do not mix identical reagents from other kits having different lot numbers. Do not use test kit reagents after the Feasibility Study has been completed.
2. Any deviation from the assay procedure may affect the results.
3. The fluorescence values may fluctuate with time; however, by using calibrators in each plate, the calculated concentrations remain constant.
4. Allow all reagents and samples to reach room temperature (+20-+25°C) before use.
5. Check that all wells have a disk after punching.
6. Discard all calibrator and control blood spot cassettes immediately after punching. Do not store them for later use. The provided reagents are intended to be used only for this feasibility evaluation study.

SUPPLIED REAGENTS

Store the reagents at +2-+8°C. Note that the calibrator and control cards should be stored at -20°C (-16 – -30°C) before opening.

GALT Calibrators

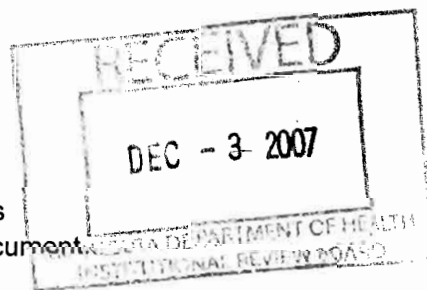
(approx. values)

Filter paper (Whatman, no. 903) cassettes containing 1 set of dried blood spots

Store frozen and protected from moisture and light in the original foil. Stable at -20°C (-16 – -30°C) for the duration of the feasibility study. Once opened, the cassette should be discarded immediately after use.

A	0	U/dL
B	1	U/dL
C	2	U/dL
D	5	U/dL
E	10	U/dL
F	18	U/dL

The exact GALT concentrations are given on the lot specific document.



GALT Controls

(approx. values)

Filter paper (Whatman, no. 903) cassettes containing 1 set of dried blood spots
Store frozen and protected from moisture and light in the original foil. Stable at -20°C (-16 – -30°C) for the duration of the feasibility study. Once opened, the cassette should be discarded immediately after use.

Normal
Abnormal

The calibrators and controls are prepared in sheep blood with GALT, phosphoglucomutase (PGM), glucose-6-phosphate dehydrogenase (G6PD) and dithiothreitol (DTT) with ProClin 300 as preservative. The hemoglobin concentration is approximately 170 g/L prior to dispensing onto Whatman, no. 903 paper.

GALT Substrate Reagent

1 vial, lyophilized
+2–+8°C until expiry date stated on the bottle label.

The reagent contains β -nicotinamide adenine dinucleotide phosphate (NADP), uridine 5'-diphosphoglucose (UDPG), galactose-1-phosphate (GAL-1-P), and dithiothreitol (DTT).

GALT Assay Buffer

1 bottle, 240 mL
+2–+8°C until expiry date stated on the bottle label.

The ready-for-use buffer contains magnesium sulfate, ethylenediaminetetraacetic acid (EDTA), tris (hydroxymethyl) aminomethane, Triton X-100 and ProClin 300 as preservative.

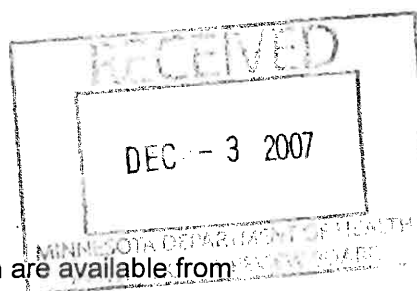
Clear microplates

(uncoated, 96 wells)
+2–+25°C

MATERIALS REQUIRED BUT NOT SUPPLIED

Using the Neonatal GALT test kit requires the following items, which are available from PerkinElmer Life and Analytical Sciences or its distributors.

1. VICTOR™ D fluorometer 1420-020 (without stacker) or 1420-021 (with stacker) plus printer and computer



2. Automatic puncher - Wallac DBS Puncher (prod. no. 1296-071) or Wallac MultiPuncher™ (prod. no. 1296-081), or a manual puncher to cut out filter paper disks with a diameter of 3.2 mm (1/8 inch)
3. Incubator capable of maintaining +37°C (e.g. Thermo iEMS Incubator/Shaker, prod. nos. 1296-009 and 1296-013 refer to 3 and 9 microplate capacity, respectively or Thermo iEMS Incubator/Shaker HT prod. no. 1296-008)
4. Plate Shaker (e.g. Wallac 1296-001 Delfia Plateshake)

In addition to the system the following are required:

- pipettes or graduated cylinders for measuring mL volumes of reagents
- 8-channel precision pipettes for dispensing 100–200 µL volumes or the Apricot Sample Processor (prod. no. MS-550XD)
- pipette tips
- reagent reservoirs
- absolute or denatured ethanol
- specimen cards using an FDA approved filter paper

WARNINGS AND PRECAUTIONS

For feasibility use only. The performance characteristics of this device has not been established. Not for use in diagnostic procedures.

This test kit should only be used by adequately trained personnel.

All equipment required for this test kit must be serviced by qualified service technicians.

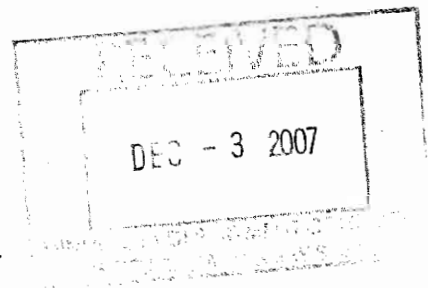
This test kit contains reagents manufactured from sheep and human blood components. The sheep are from a closed herd located in the USA. The human blood has been tested using FDA approved methods or equivalent, and found to be negative for hepatitis B surface antigen, anti-hepatitis C and anti-HIV 1 and 2 antibodies. Nevertheless, all recommended precautions for the handling of blood derivatives should be observed. Please refer to the U.S. Department of Health and Human Services publication "Biosafety in Microbiological and Biomedical Laboratories" or any other local or national regulation.

Handle all patient specimens as potentially infectious.

All the reagents may be irritating.



Follow local regulations for handling of ethanolic solutions.

Disposal of all waste should be in accordance with local regulations.

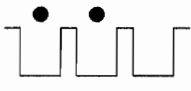
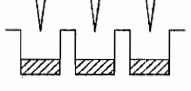
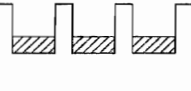
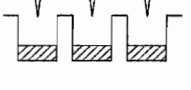


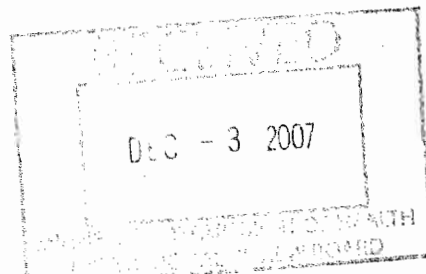
Neonatal GALT Test Kit SUMMARY PROTOCOL SHEET

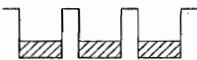
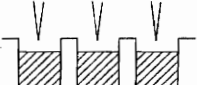

REAGENT PREPARATION

Reconstitute GALT Substrate Reagent		2.8 mL of deionized water, 5 min – 1 week before use
Dilute Necessary Amount of GALT Substrate to Assay Buffer		Reconstituted Substrate into GALT Assay Buffer, 5 – 60 min before use

ASSAY PROCEDURE

Punch out calibrators, controls and unknowns		Use the clear microplate included in the test kit
Add GALT Assay Buffer		25 μ L, shake the plate 30 sec to mix
Incubate		10 min at +37°C
Add Substrate Reagent in GALT Assay Buffer		80 μ L, shake the plate 30 sec to mix



Incubate		2 h (± 30 min.) at +37°C
Add GALT Assay Buffer		100 µL, shake the plate 2 min to mix
Measure		(355 nm excitation, 460 nm emission)

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MINNESOTA DEPARTMENT OF HEALTH
PUBLIC HEALTH DIVISION



Protecting, maintaining and improving the health of all Minnesotans

October 6, 2008

Amy Hietala
Minnesota Department of Health Lab
601 Robert Street North
St. Paul, MN 55164

Re: IRB #07-187

IRB Original Review Date: December 27, 2007

Re-Review due in IRB Administrative Office: File Closed

Approval Expires: File Closed October 6, 2008

Dear Amy:

Thank you for submitting the Re-Review form for your proposal IRB #07-187 entitled "New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study" to the Minnesota Department of Health's Institutional Review Board (IRB) for review.

On the form you indicated that the project is no longer in progress. Because of this the file on this project will be officially closed on October 6, 2008.

Cordially,

A handwritten signature in black ink that reads "Peter Rode". The signature is written in a cursive style with a large, looping initial "P".

Peter Rode
IRB Administrator
651/201-5942

cc:
Ann Kowski

RE-REVIEW CHECKLIST

Approval Expiration Date: December 27, 2008

Item	Answer / Explanation		
IRB Project #	07-187		
Protocol Title	New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study		
Principal Investigator	Amy Hietala		
Project Description	MDH Newborn Screening Program in collaboration with Perkin Elmer Life & Analytical Sciences (PE) is prosing to demonstrate equivalence or superiority between two assays for performance and specimen results in the determination of Galactose-1 Phosphate Uridyl Transferase (GALT) activity in neonatal diagnostic dried blood spot specimens. Galactosemia is one of the 54 disorders on Minnesota's screening panel.		
Date of Original Review:	December 27, 2007		
Previous type of Review	Exempt <input checked="" type="checkbox"/> Expedited <input type="checkbox"/> Full Board <input type="checkbox"/>		
Previous Primary Reviewer (if any)	Peter Rode		
Met all Stipulations?	YES <input type="checkbox"/>	NO <input type="checkbox"/>	Not Applicable <input checked="" type="checkbox"/>
Dates of Re-Review	First		
Project Status	OPEN <input type="checkbox"/>	CLOSED <input checked="" type="checkbox"/>	OTHER <input type="checkbox"/>
Major Changes?	YES <input type="checkbox"/> NO <input type="checkbox"/>		

Action Needed:

- Review by Administration only (report to Board)
- Expedited Review (report to Board)
 - Review by Original Primary Reviewer: _____
- Review by Full Board (full Board votes)
 - Primary Reviewer: _____
- Send to Data Practices Office?

<input type="checkbox"/>	Staff Recommendation:
Close file. <i>OK PR</i>	



**MINNESOTA DEPARTMENT OF HEALTH
 INSTITUTIONAL REVIEW BOARD
 P.O. Box 64882
 ST. PAUL, MN 55164-0882
 Re-Review of Exempt Research**

Instructions: Use this form when submitting a request for re-review of a protocol with exemption from 45 CFR 46. Please send the **signed** original to the IRB Administrative Office at the address listed above. Complete all applicable items **and** sign the form or it will be returned to you.

New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study 07-187

Title of Study or Project IRB Identification Number

MDH Newborn Screening Program in collaboration with Perkin Elmer Life & Analytical Sciences (PE) is prosing to demonstrate equivalence or superiority between two assays for performance and specimen results in the determination of Galactose-1 Phosphate Uridyl Transferase (GALT) activity in neonatal diagnostic dried blood spot specimens. Galactosemia is one of the 54 disorders on Minnesota's screening panel

Project Description

December 27, 2007 First November 12, 2008

Date of Initial IRB Review/Exemption Last Re-Review Date Next Scheduled IRB Review

Check if PI has changed

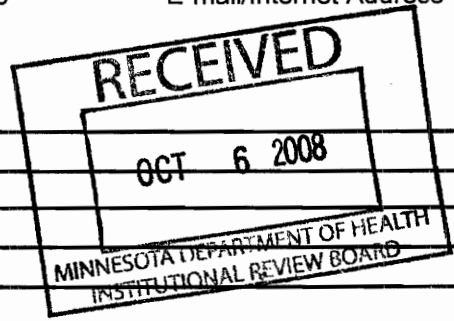
Amy Hietala 651-201-5455 651-201-5465

Name of Principal Investigator Phone Number Fax Number

601 Robert Street North St. Paul, MN 55164 amy.hietala@state.mn.us

Address (Street or P.O. Box) City State & Zip E-mail/Internet Address

List Below names of other MDH Employee Co-investigators:



1. Is the study or project still active? Yes No

1a. If still active: What stage is the project in?

Finalizing design and procedures Data analysis

Data collection
 Other (explain): _____

report writing

2. Have there been any changes in the study's objectives, methods, or subjects?

Yes, If yes, please describe below **and** submit 3 unbound copies of the revised protocol.

No

3. Have there been any changes in the study's informed consent process or forms?

Yes, If yes, please describe below **and** submit 3 unbound copies of the current consent form(s).

No

4. Have there been any adverse events or unanticipated problems involving risks to subjects or others, any withdrawal of subjects from the research, or complaints about the research?

Yes, If yes, please describe below.

No

4a. Have these events been reported to the IRB or other authorities? *Not Applicable*

Yes, If yes, date reported: _____ reported to: _____

No

<i>Amy Pietala</i> Newborn Screening Laboratory Supervisor	9-27-2008
PI Signature and Position Title	Date



Ann Kowski - Re: 2008 Re-review of IRB #07-187

From: Amy Hietala
To: Ann Kowski
Date: 09/27/2008 12:40 PM
Subject: Re: 2008 Re-review of IRB #07-187

Hello Ann:

I am interoffice mailing you the form. Please let me know if you have not received it by 10/2. Thanks!

Amy

>>> Ann Kowski 9/23/2008 12:48 PM >>>

Your project, IRB #07-187 entitled "New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study", was found to be exempt from full board review on December 5, 2007, and is due for re-review during the November 12, 2008, meeting.

Attached is a Re-review form for you to complete, sign, and mail back to me **no later than October 17, 2008**. My address is IRB, 85 East Seventh Place, Golden Rule Building, Suite 300, St. Paul, MN 55164.

This form will need to be completed and sent in even if your project has closed since it was last reviewed. If this is the case, please indicate that on the form by checking by "Project is no longer in progress".

MDH will stop using "health" in its e-mail addresses this fall. Please use my new-email address: ann.kowski@state.mn.us.

Thanks, and have a great day.

**Ann Kowski
Institutional Review Board Coordinator
Minnesota Department of Health
85 East Seventh Place, PO 64882
Golden Rule Building, Suite 300
St. Paul, MN 55164-0882
651-201-5940
Fax: 651-201-5179**

Ann Kowski - 2008 Re-review of IRB #07-187

From: Ann Kowski
To: Amy Hietala
Date: 09/23/2008 12:48 PM
Subject: 2008 Re-review of IRB #07-187
Attachments:

Your project, IRB #07-187 entitled "New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study", was found to be exempt from full board review on December 5, 2007, and is due for re-review during the November 12, 2008, meeting.

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MDH will stop using "health" in its e-mail addresses this fall. Please use my new-email address: ann.kowski@state.mn.us.

Thanks, and have a great day.

**Ann Kowski
Institutional Review Board Coordinator
Minnesota Department of Health
85 East Seventh Place, PO 64882
Golden Rule Building, Suite 300
St. Paul, MN 55164-0882
651-201-5940
Fax: 651-201-5179**



December 5, 2007

Protecting, maintaining and improving the health of all Minnesotans

Amy Hietala
Minnesota Department of Health
601 Robert Street North
St. Paul, MN 55155

RE: IRB #07-187

Original IRB Review Date: December 5, 2007

Re-review due in IRB Administrative Office: October 9, 2008

IRB Approval Expires: December 5, 2008

Dear Amy:

Thank you for submitting your proposal entitled "New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study" to the Minnesota Department of Health's (MDH) Institutional Review Board (IRB) for review.

We have reviewed your proposal and determined that it is exempt from IRB review in accordance with 45 CFR 46.101(b)(4) ("*Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or the information is recorded by the investigator in such a manner that subjects cannot be identified, directly, or through identifiers linked to the subjects.*").

As Principal Investigator of this project you are required by federal regulations to inform the IRB of any proposed changes in your research that will affect human subjects. Changes should not be initiated until written IRB approval is received. Adverse events must be reported to the Board as they occur. Research projects are subject to continuing review and renewal. You will receive a Re-review form approximately one month prior to the approval expiration date noted above.

Please note that your project has been assigned a five-digit code number (above). Please use this five-digit code number **and** the title of your study in all future communications with the IRB office.

Sincerely,

A handwritten signature in black ink that reads "Peter Rode". The signature is written in a cursive, flowing style.

Peter Rode
IRB Administrator
PO Box 64882
St. Paul, MN 55164-0882
651-201-5942

cc: Ann Kowski

From: Rita Messing
To: Peter Rode; Richard Danila
Date: 12/05/2007 11:42 AM
Subject: Re: IRB 07-187

CC: Ann Kowski

Looks exempt to me. It seems to be covered by the newborn screening program franchise, and the spots are de-identified.

Rita B. Messing, Ph.D., Supervisor
Site Assessment and Consultation Unit
Division of Environmental Health
Minnesota Department of Health
625 N. Robert St.
St. Paul, MN 55155-2538
Telephone: (651)201-4916
Fax: (651)201-4606

>>> Peter Rode 12/4/2007 3:13 PM >>>
Hi, Rich and Rita:

This study is titled "New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study", and the PI is Amy Hietala. This study will test two different ways of detecting "GALT activity" in neonatal dried blood specimens to determine if they are equivalent or if one is superior. The study will use de-identified dried blood spots from the MDH newborn screening program. The lab testing will be done here at MDH. One test method has already been used when the dried blood spots were first analyzed. The 2nd test will be applied to residual blood spots from the same infants, and the results will be compared. The de-identified results of these tests will be shared with the manufacturer of the 2nd test kit, PerkinsElmer of Finland.

This is very similar to an earlier study, 07-155, that also compared two different test kits for another newborn disorder using dried blood spots. Because the dried blood spots are de-identified and there is no analysis or sharing of personal identifiers or of demographics, I feel this study is exempt under category 4.

Let me know what you think or if you have any questions.

Pete

Pete Rode
Center for Health Statistics
85 East 7th Place, 3rd Floor
P.O. Box 64882
St. Paul, MN 55164-0882

(651) 201-5942

(651) 201-5179 (fax)

peter.rode@health.state.mn.us

From: Peter Rode
To: Richard Danila; Rita Messing
Date: 12/04/2007 3:13 PM
Subject: IRB 07-187

CC: Ann Kowski
Hi, Rich and Rita:

This study is titled "New GALT (Galactose-1 Phosphate Uridyl Transferase) Feasibility Study", and the PI is Amy Hietala. This study will test two different ways of detecting "GALT activity" in neonatal dried blood specimens to determine if they are equivalent or if one is superior. The study will use de-identified dried blood spots from the MDH newborn screening program. The lab testing will be done here at MDH. One test method has already been used when the dried blood spots were first analyzed. The 2nd test will be applied to residual blood spots from the same infants, and the results will be compared. The de-identified results of these tests will be shared with the manufacturer of the 2nd test kit, PerkinsElmer of Finland.

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Let me know what you think or if you have any questions.

Pete

Pete Rode
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