[reviewer notes¬]

## Provide a short title for this study (200 characters or less):

**Clinical and Predictive Assessment of Patients With Chronic Liver Diseases**

**T1.0** ## Select the type of application:

New Research Study

**T2.0** ## Is the proposed research study limited to the inclusion of deceased individuals?

* No

The review and approval of proposed innovative practices are ***not*** subject to IRB review and approval. The introduction of innovative procedures or therapies into clinical practice (i.e., independent of a research activity approved by the IRB) should be reviewed with the applicable department chairperson and the UPMC Technology Assessment Committee/Innovative Practices Sub-Committee prior to their implementation. The contact person is **Mary Gardner at 412-647-6883.**

**T2.1**

## Are any research activities being conducted at the VA Pittsburgh Healthcare System or with VA funds?

* No

Respond to the following questions to determine the IRB-of-record:

**Research is conducted using only VA records and/or subjects recruited thru the VA:**
**University or UPMC facilities are not engaged in research:**
**University or UPMC funds are not expended in direct support of research:**

If all **true**, then the VA is the IRB-of-record and UPitt IRB review is not required.
If all **false**, only UPitt IRB review is required.
Otherwise, dual review from both the VA and UPitt IRB is required.

**Please select the external IRB of record:**

## Provide the name of the Central IRB:

Quality assurance projects are ***not*** subject to IRB review and approval. UPMC has adopted an oversight process that requires the submission of all quality assurance projects for review. At UPMC, submissions are reviewed by the Quality Improvement Review Committee (QRC). You can contact the QRC at askqrc@upmc.edu.

Research studies that are limited to the inclusion of deceased individuals are ***not*** subject to IRB review and approval. Research performed on individuals who have been declared legally dead and/or research involving the collection of tissues from deceased individuals is not subject prior review and approval by the University of Pittsburgh IRB.

There are, however, ethical issues associated with research conducted on or involving deceased individuals. To address these ethical issues, all University faculty who desire to perform research on or involving deceased individuals must submit a project application for review and approval by the Committee for Oversight of Research and Clinical Training Involving the Dead Research Involving the Dead (CORID). Note that, as per UPMC policies, research involving the medical records of deceased individuals is subject to obtaining the written consent of the decedentsâ€™ next-of-kin or the executors of the decedentsâ€™ estates.

For studies that include **BOTH** living and deceased subjects, IRB review and approval **is required**.

Emergency Use is the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval [21 CFR312.310]. Detailed information on the submission process is available on the IRB website under the A-Z Guidance, Emergency Use.

## All of the following conditions must exist to justify the emergency use of an unapproved investigational drug, biologic, or device. Check all the boxes that apply:

Selections

There are no items to display

[reviewer notes¬]

**T3.0** **What is the anticipated risk to the research participants?**

Minimal Risk

**T3.1** **Why do you feel that all aspects of this research study, including screening and follow-up, involve no more than minimal risk to the research subjects?**

This project involves retrospective and prospective collection of medical record information. All of the data being used for this project contains information to which the investigators already have clinical access. The only foreseeable risk is breach of confidentiality, as can occur with any research, and we will make all efforts to secure information used for research.

**T4.0** **Does the proposed study qualify for 'exempt' IRB review or for a determination of either 'not research' or 'no human subject' involvement?**

* No

**T5.0** **Does the proposed research study qualify for 'expedited' IRB review status?**

* Yes

Section: Cover Sheet

[reviewer notes¬]

**CS1.0** **What is the reason for this submission?**

New Research Protocol Submission

**CS1.1** **Has this research study been approved previously by the University of Pittsburgh IRB?**

* No

If the **study expired**, you are required to upload the completed Renewal Report Form and a Data and Safety Monitoring Report.

Upload the Renewal Report Form and Data and Safety Monitoring Report:

| Name | Modified Date |
|---|---|

Previous IRB #:

**CS1.1.1** **Has this research study (or a substantially similar research study) been previously disapproved by the University of Pittsburgh IRB or, to your knowledge, by any other IRB?**

* No

If **Yes**, identify the IRB, IRB number if Pitt IRB disapproved, and the primary reasons for disapproval:

[reviewer notes¬]

**CS2.0** **Title of Research Study:**

**Clinical and Predictive Assessment of Patients With Chronic Liver Diseases**

**CS2.0.1**

## Requested approval letter wording:

**CS2.1** **Research Protocol Abstract:**

Medical record information collected for clinical use offers benefits for use in research. Analyzing medical record information collected for clinical purposes could help the researchers involved in this project answer the research questions posed. All of the data are those to which the investigators already have clinical access. We will review the electronic clinical records of patients seen in the Center for Liver Diseases and the Starzl Transplant Institute in order to discover how to use clinical information to diagnose and predict the outcome of complex liver diseases and their potential for cure or improvement with new forms of treatment.

We will not use the requested IRB project approval to cover the following categories of reviews:
Chart reviews where data will be sent to a national or multicenter database/registry
Chart reviews that have outside funding
Chart reviews for those individuals who want their own IRB approval letter with them listed as PI
Chart reviews that fall outside of the specific aims of this chart review study

**CS2.2** **Select the category that best describes your research:**

[reviewer notes¬]

**CS3.0** **Name of the Principal Investigator:**

Michael Dunn

Note: Adjunct faculty of the University, including lecturers and instructors, are not permitted to serve as a PI or Faculty Mentor but may serve as co-investigators. Refer to Chapter 4 on the HRPO website for more information.

**CS3.1** **Affiliation of Principal Investigator:**

UPitt faculty member

If your answer was **Other**, fill in the Principal Investigator's affiliation:

If you chose any of the **Pitt options**, please indicate the specific campus:
Main Campus - Pittsburgh

If you chose the UPitt faculty member option, provide the PIâ€™s **University Faculty Title**:

**CS3.1.1** **Indicate below the name of the qualified University faculty member or UPP or UPMC staff member who will serve as a mentor and provide supervision or guidance regarding the conduct of this research study.**

**CS3.2** **Address of Principal Investigator:**

Division of Gastroenterology, Hepatology and Nutrition
University of Pittsburgh School of Medicine
200 Lothrop St. - PUH, M2, C-wing
Pittsburgh, PA 15213

**CS3.3** **Recorded Primary Affiliation of the Principal Investigator:**

U of Pgh | School of Medicine | Medicine

**CS3.4** **Identify the School, Department, Division or Center which is responsible for oversight of this research study:**

U of Pgh | School of Medicine | Medicine | Gastroenterology

**CS3.5** **Telephone Number of Principal Investigator:**

412-692-2470, mobile 814-241-7546

**CS3.6** **Recorded Current E-mail Address of Principal Investigator to which all notifications will be sent:**

dunnma@upmc.edu

**CS3.7** **Fax Number:**

412-647-9268

**CS3.8** **Does this study include any personnel from Carnegie Mellon University, and/or use any CMU resources or facilities (e.g., Scientific Imaging and Brain Research Center (SIBR)?**

* No

**CS3.9** **Is this your first submission, as PI, to the Pitt IRB?**

* No

[reviewer notes¬]

**CS4.0** **List of Co-Investigators:**

| Last | First | Organization |
|---|---|---|
| Andrzejewski | Margaret | UPMC \| Physician Services Division \| UPP \| Other |
| Bataller | Ramon | U of Pgh \| School of Medicine \| Medicine |
| Behari | Jaideep | U of Pgh \| School of Medicine \| Medicine |
| Bloomer | Pamela | UPMC \| Hospital Divisions \| Presbyterian/Shadyside \| Medicine |
| Chopra | Kapil | U of Pgh \| School of Medicine \| Medicine |
| Dapice | Anjouli | UPMC \| Physician Services Division \| UPP \| T.E. Starzl Transplantation Institute |
| Demetris | Anthony | U of Pgh \| School of Medicine \| Pathology |

| | | |
|---|---|---|
| Dimartini | Andrea | U of Pgh \| School of Medicine \| Psychiatry |
| Donovan | Becky | Other |
| Furlan | Alessandro | U of Pgh \| School of Medicine \| Radiology |
| Ganesh | Swaytha | U of Pgh \| School of Medicine \| Medicine |
| Gironda | Patricia | Other |
| Graham | Lisa | UPMC \| Hospital Divisions \| Presbyterian/Shadyside \| Medicine \| Gastroenterology |
| Greer | Julia | U of Pgh \| School of Medicine \| Medicine |
| Hughes | Christopher | U of Pgh \| School of Medicine \| Surgery |
| Humar | Abhinav | U of Pgh \| School of Medicine \| Surgery |
| Jazwinski | Alison | U of Pgh \| School of Medicine \| Medicine |
| Jonassaint | Naudia | U of Pgh \| School of Medicine \| Medicine |
| Lippello | Anita | UPMC \| Hospital Divisions \| Presbyterian/Shadyside \| Medicine \| General Internal Medicine |
| Luce | Marybeth | UPMC |
| Malik | Shahid | U of Pgh \| School of Medicine \| Medicine \| Gastroenterology |
| Manfredi | Amy | UPMC \| Hospital Divisions \| Presbyterian/Shadyside \| UPMC Surgery |
| Rabinovitz | Mordechai | U of Pgh \| School of Medicine \| Medicine |
| Rachakonda | Vikrant | U of Pgh \| School of Medicine \| Medicine |
| Schmotzer | Amy | UPMC \| Physician Services Division \| UPP \| Medicine |
| Shaikh | Obaid | U of Pgh \| School of Medicine \| Medicine |
| Tevar | Amit | U of Pgh \| School of Medicine \| Surgery |
| Tsung | Allan | U of Pgh \| School of Medicine \| Surgery \| General Surgery |
| Yuan | Jian-Min | U of Pgh \| Graduate School of Public Health \| Epidemiology |

[reviewer notes¬]

**CS5.0** **Name of Primary Research Coordinator:**

Amy Schmotzer

**CS5.1** **Address of Primary Research Coordinator:**

Center for Liver Diseases
3471 Fifth Avenue
Suitre 916
Pittsburgh, PA 15213

**CS5.2** **Telephone Number of Primary Research Coordinator:**

**412-802-8567**

**CS6.0** **Name of Secondary Research Coordinator:**

**CS6.1** **Address of Secondary Research Coordinator:**

**CS6.2** **Telephone Number of Secondary Research Coordinator:**

**CS6.3** **Key Personnel/Support Staff (Only list those individuals who require access to OSIRIS):**

| Last | First | Organization |
|---|---|---|
| There are no items to display | | |

[reviewer notes¬]

**CS7.0** **Will this research study use any Clinical and Translational Research Center (CTRC) resources?**

No

**CS7.1** **Please select the sites you intend to use:**

There are no items to display

[reviewer notes¬]

**CS8.0** **Select the entity responsible for scientific review.**

**Department Review** - (a dean, department chair, division chief, or center head)
Note: **DoD funded studies** require departmental review

**CS8.1** **Select the school, department or division which is responsible for scientific review of this submission.**

U of Pgh | School of Medicine | Medicine | Gastroenterology

**CS8.1** **Select the CTRC which is responsible for scientific review of this submission**

[reviewer notes¬]

**CS9.0** **Does this research study involve the administration of an investigational drug or an FDA-approved drug that will be used for research purposes?**

* No

**CS9.1** **Do you plan to utilize the Investigational Drug Service (IDS) to dispense the drug?**

*

**CS10.0** **Is this research study being conducted under a University of Pittsburgh-based, sponsor-investigator IND or IDE application?**

* No

*If YES, you are required to submit the IND or IDE application and all subsequent FDA correspondence through the Office for Investigator-Sponsored IND and IDE Support (O3IS). Refer to applicable University policies posted on the O3IS website (www.O3IS.pitt.edu).*

**CS10.1** **Append to this application**:

(1) Copy of the current version of the clinical protocol submitted with the IND or IDE application which corresponds to this IRB submission:
Name Modified Date

(2) Copy of the FDAâ€™s letter which acknowledges receipt of the application and assignment of the IND or IDE number:

Name Modified Date

[reviewer notes¬]

**CS11.0** **Use the 'Add' button to upload one or more of the following:**

- **the sponsor protocol (including investigator initiated studies) and/or other brochures**
- **the multi-center protocol and consent form template, *if applicable***

Name Modified Date

**Is this research study supported in whole or in part by industry? This includes the provision of products (drugs or devices).**

* No

**Is this a multi-centered study?**

* No

[reviewer notes¬]

**CS12.0** **Does your research protocol involve the evaluation or use of procedures that emit ionizing radiation?**

*

## HUSC GUIDANCE
## REQUIREMENTS FOR THE REVIEW OF HUMAN SUBJECT RESEARCH PROTOCOLS BY THE HUMAN USE SUBCOMMITTEE (HUSC), RADIATION SAFETY COMMITTEE (effective 7/1/2018)

For Research Protocols Involving the Use or Evaluation of **Diagnostic or Therapeutic Procedures** that Emit Ionizing Radiation:

â€¢ Formal HUSC review/approval is required if the:

1. research protocol involves the use or the evaluation (i.e., for safety and/or effectiveness) of a radioactive agent or a device that is not currently FDA-approved for commercial marketing; including radioactive drugs or devices that are the subject of a FDA-accepted IND or IDE application or approved for clinical investigations under the FDAâ€™s Radioactive Drug Research Committee (RDRC) process. [1]
2. research protocol addresses (i.e, in the objectives or specific aims) the evaluation (i.e., for safety and/or effectiveness) or involves the use of a FDA-approved radiopharmaceutical or device-associated procedure for an â€œexperimentalâ€ indication or using â€œexperimentalâ€ procedures (i.e., an indication or procedures that are not consistent with standard clinical practice or the current FDA-approved product labeling). [1]
    - Note: HUSC review/approval is not required for research protocols that involve the use of diagnostic procedures being performed, in a manner and frequency that are consistent with standard clinical practice, for subject screening or to evaluate the outcome of a treatment regimen. This would include diagnostic procedures for off-label uses that are routinely performed in clinical practice. [1,2,3]
    - Note: HUSC review/approval is not required for research protocols that involve the use of therapeutic procedures being performed in a manner and frequency that is consistent with standard clinical practice. [1,2,3]
3. research protocol involves the enrollment of individuals (e.g., healthy volunteers) who will not be undergoing the procedure in association with the diagnosis or treatment of a disease or condition. [1]

For Humanitarian Use Devices:

â€¢ Formal HUSC review/approval is required for all Humanitarian Use Devices that emit ionizing radiation.

For any questions related to these requirements or their application, contact the Chair of the HUSC (412-647-0736) or the Universityâ€™s Radiation Safety Officer (412-624-2728).

[1] All research protocols wherein the parameters (e.g., dose, dosing frequency) for performing the procedure(s) that emit ionizing radiation are defined in the protocol must include an Authorized User (i.e., a physician or dentist who has expertise and who is credentialed in the respective medical specialty) as a listed co-investigator; i.e., so as to ensure adequate notification and respective compliance with the protocol.
[2] The risks of radiation exposure associated with the diagnostic or therapeutic procedure must continue to be addressed in the protocol and consent form using the standard, HUSC-accepted wording. (For diagnostic procedures refer to the University Human Research Protection Office website â€“ www.hrpo.pitt.edu: A-Z Guidance/Radiation Guidance. For therapeutic procedures, address the specific risks currently known to be associated with the respective procedure.
[3] The University of Pittsburgh IRB, at its discretion, may request formal HUSC review of the research protocol.

**CS12.1** **After reviewing the HUSC guidance above, does your research protocol require HUSC review?** (Note: University of Pittsburghâ€™s Radiation Safety Committee oversight is limited UPMC Presbyterian-Shadyside, Magee Womenâ€™s Hospital of UPMC, Childrenâ€™s Hospital of Pittsburgh-UPMC, and Hillman Cancer Center. If other sites, you will be required to obtain approval from your radiation safety officer. Please contact askirb@pitt.edu for more information.)

No

Upload Radiation Forms:

| Name | Modified Date |
|---|---|

**CS13.0** **Does this research study involve the deliberate transfer of recombinant or synthetic nucleic acid molecules into human subjects?**

* No

Upload Appendix M of NIH Guidelines:

| Name | Modified Date |
|---|---|

**CS14.0** **Are you using UPMC facilities and/or UPMC patients during the conduct of your research study?**

* No

If Yes, upload completed Research Fiscal Review Form:

| Name | Modified Date |
|---|---|

[reviewer notes¬]

**CS15.0** **Indicate the sites where research activities will be performed and/or private information will be obtained.**

Choose all sites that apply and/or use **Other** to include sites not listed:

Sites:
University of Pittsburgh
UPMC

**University of Pittsburgh**
Campus:
Main Campus - Pittsburgh

List university owned off-campus research sites if applicable:

**UPMC**
Sites:
UPMC Presbyterian
UPMC Shadyside

**UPMC Cancer Network Sites:**
Site
There are no items to display

If you selected **School**, **International** or **Other**, list the sites:

***For research being conducted at non Pitt or UPMC sites, upload a site permission letter granting the researcher permission to conduct their research at each external site:**
Name Modified Date

**CS15.1** **Have you, Michael Dunn , verified that all members of the research team have the appropriate expertise, credentials, and if applicable, hospital privileges to perform those research procedures that are their responsibility as outlined in the IRB protocol?**

* Yes

**CS15.2** **Describe the availability of resources and the adequacy of the facilities to conduct this study:**

* The Principal Investigator as well as the co-investigators in this department conduct IRB-approved research on a routine basis. They have access to UPMC records.
The PI has sufficient time to oversee and train the research staff for this study.

The PI has sufficient staffing, including a full-time coordinator and also a designated UPMC report writer to assist with gathering information when needed.
All study staff have completed all required research modules.
The PI has adequate funding to complete this study.
The PI has access to protected servers to insure data security for generated, collected, and stored data. Data are stored on password-protected systems.
The PI has adequate space within UPMC to conduct this research.
This is a study of retrospective and prospective data review. There is no need for addiitonal medical and/or psychological resources.

[reviewer notes¬]

**CS16.0 Special Research Subject Populations:**

| Categories |
| --- |
| None |

[reviewer notes¬]

**CS17.0 Does your research involve the experimental use of any type of human stem cell?**

* No

[reviewer notes¬]

**NIH Definition of a Clinical Trial**

***A research study[1] in which one or more human subjects[2] are prospectively assigned[3] to one or more interventions[4] (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.[5]***

[1] See Common Rule definition of research at 45 CFR 46.102(d) .

[2] See Common Rule definition of human subject at 45 CFR 46.102(f) .

[3] The term â€œprospectively assignedâ€□ refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

[4] An intervention is defined as a manipulation of the subject or subjectâ€™s environment for the purpose of modifying one or more health-related biomedical or

behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

[5] Health-related biomedical or behavioral outcome is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjectsâ€™ biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

**CS18.0** * **Based on the above information, does this study meet the NIH definition of a clinical trial?**
( )( )Yes ( )( )No

If Yes, click Save and then Click Here For Study Team's CITI Training Records . Please ensure all personnel's training is up to date

| | Section: Section 1 - Objective, Aims, Background and Significance |
|---|---|

[reviewer notes¬]

**1.1** **Objective: What is the overall purpose of this research study?** (Limit response to 1-2 sentences.)
The objective is to evaluate present methods and to determine new methods for the treatment and cure of complex liver disease. We will review the electronic clinical records of patients seen in the Center for Liver Diseases and the Starzl Transplant Institute in order to discover how to use clinical information to diagnose and predict the outcome of complex liver diseases and their potential for cure or improvement with new forms of treatment.

**1.2** **Specific Aims: List the goals of the proposed study (e.g., describe the relevant hypotheses or the specific problems or issues that will be addressed by the study).**
The goals of the proposed study are to gather information about liver disease to contribute to better understanding of how and when the disease progresses. We will review the electronic clinical records of patients seen in the Center for Liver Diseases and the Starzl Transplant Institute in order to discover how to use clinical information to diagnose and predict the outcome of complex liver diseases and their potential for cure or improvement with new forms of treatment.

The scope of our intended record reviews would encompass the multiple types of information gathered from medical records of the large patient population of over 200,000 persons seen in the past, as well as those presently seen, and those who will be seen in the future at the Center for Liver Diseases and the Starzl Transplant Institute. Analysis of many categories of information has proven to be essential for developing new diagnostic strategies and new prediction of clinical outcomes in complex liver diseases.

Specific aims:
1. Evaluate indices derived from common laboratory tests, such as the AST:ALT Ratio and the AST:Platelet Ratio Index that can help predict the clinical risk of adverse outcomes in nonalcoholic fatty liver disease as well as the presence of scarring, or fibrosis, on a liver biopsy.

2. Determine the presence, duration and severity of key symptoms such as chronic pain that may correlate with poor outcomes after transplantation, or itching that can predict bile duct involvement in biliary cirrhosis or sclerosing cholangitis.

3. Assess the extent of key physical measurement abnormalities such as high blood pressure associated with polycystic liver and kidney disease, weight gain associated with fatty liver disease, and weight loss associated with neoplasms and inflammatory conditions, and when such changes should trigger further testing and evaluation based on their duration or severity.

4. Explore the association of commonly used medications with unexpected forms of liver injury, for example, the finding that the cardiac drug amiodarone can cause severe fatty liver disease.

5. Explore new disease associations, such as the occurrence of arthritis and immune complex mediated rashes in persons infected with hepatitis C, and their improvement with antiviral therapy.

6. Discover both unexpectedly favorable treatment outcomes and unexpected adverse effects of new medications, such as the new generation of antiviral medications for hepatitis C, that will lead to adjustment in treatment programs and development of even more effective treatments.

**1.3 Background: Briefly describe previous findings or observations that provide the background leading to this proposal.**

Clinical research is grounded in clinical experience. Organizing, aggregating and analyzing clinical data from medical records, our core approach, has been the primary process that has allowed generation of hyptheses from clinical experience for further validation and prospective testing.

The initial recording of data in elecronic medical records was first intended to support the capture of workload, coding and billing for the business processes of patient care. It is now evident that this same information, recorded and used for documentation of the care of individual patients, has the capacity to contribute to medical knowledge when it is captured, aggregated and analyzed as described in 1.2 above. Center for Liver Diseases and Starzl Transplant Institute investigators have shown the ability to generate new clinical knowledge and to generate hypotheses for prospective testing by review of clinical data, for example, on the risk of liver cancer in nonalcoholic fatty liver disease and on the prospects for success with new therapy for chronic hepatitis C.

**1.4 Significance: Why is it important that this research be conducted? What gaps in existing information or knowledge is this research intended to fill?**

The scope of our intended record reviews would encompass the multiple types of information gathered from medical records of the large patient population of over 200,000 persons seen in the past, those presently seen and those who will be seen in the future at the Center for Liver Diseases and the Starzl Transplant Institute. Analysis of many categories of information has proven to be essential for developing new diagnostic strategies and new prediction of clinical outcomes in complex liver diseases.

Discovery of both unexpectedly favorable treatment outcomes and unexpected adverse effects of new medications, such as the new generation of antiviral medications for hepatitis C, that will lead to adjustment in treatment programs and development of even more effective treatments.

Section: Section 2 - Research Design and Methods

[reviewer notes¬]

**2.1** **Does this research study involve the *use* or evaluation of a drug, biological, or nutritional (e.g., herbal or dietary) supplement?**

* No

**2.1.1** **Does this research study involve an evaluation of the safety and/or effectiveness of one or more marketed nutritional (e.g., herbal or dietary) supplements for the diagnosis, prevention, mitigation or treatment of a specific disease or condition or symptoms characteristic of a specfic disease or condition?**

*

**2.1.1.1** **List each of the marketed nutritional supplements being evaluated in this research study. Specify for each supplement the corresponding IND number or attach FDA correspondence specifying that an IND is not required.**

| Marketed nutritional supplement | IND number |
|---|---|
| There are no items to display | |

**Upload FDA correspondence specifying that an IND is not required, if applicable:**

| Name | Modified Date | Version |
|---|---|---|

[reviewer notes¬]

**2.2** **Will this research *use* or evaluate the safety and/or effectiveness of one or more devices?**

* No

**2.2.1** **Does this research study involve an evaluation of the safety and/or effectiveness of one or more devices not currently approved by the FDA for general marketing?**

*

If **YES**, describe your **plan to prevent unauthorized use of the investigational device**:

**2.2.1.1** **List each of the unapproved devices being evaluated in this research study.**

Specify for each listed device the corresponding Investigational Device Exemption (IDE) number or provide a justification for why you feel that this device and its use, as proposed in this research study constitute a non-significant risk (i.e., to include potential failure of the device) to the research subjects:

| Unapproved device | IDE # | Non-significant risk justification |
|---|---|---|
| There are no items to display | | |

[reviewer notes¬]

**2.3** **Summarize the general classification (e.g., descriptive, experimental) and methodological design (e.g., observational, cross-sectional, longitudinal, randomized, open-label single-blind, double-blind, placebo-controlled, active treatment controlled, parallel arm, cross-over arm) of the proposed research study, as applicable.**

Thi project is observational as it involves chart review/review of medical record information of all patients followed in the Center for Liver Diseases and the Starzl Transplant Institute.

**2.3.1** **Does this research study involve a placebo-controlled arm?**

* No

[reviewer notes¬]

**2.4** **Will any research subjects be withdrawn from known effective therapy for the purpose of participating in this research study?**

* No

**2.4.1** **Provide a justification for discontinuing subjects from known effective therapy for the purpose of study participation.**

**2.4.2** **Describe the risks to subjects associated with discontinuing them from known effective therapy for the purpose of study participation.**

[reviewer notes¬]

**2.5** **Will screening procedures (i.e., procedures to determine research subject eligibility) be performed specifically for the purpose of this research study?**

* No

**2.5.1** **List the screening procedures that will be performed for the purpose of this research study. Do NOT include the inclusion/exclusion criteria in this section as they will be addressed in section 3; questions 3.13 and 3.14.**

**2.5.2** **What steps will be taken in the event that a clinically significant, unexpected disease or condition is identified during the conduct of the screening procedures?**

Not Applicable

[reviewer notes¬]

**2.6** **Provide a detailed description of all research activities (e.g., all drugs or devices; psychosocial interventions or measures) that will be performed for the purpose of this research study.**

This description of activities should be complete and of sufficient detail to permit an assessment of associated risks.

At a minimum the description should include:

- **all research activities**
- **personnel (by role) performing the procedures**
- **location of procedures**
- **duration of procedures**
- **timeline of study procedures**

UPMC report writers via CARe (Center for Assistance in Research using eRecord) are routinely used for retrospective studies done in our Division. We are asking for those same individuals, as well as the investigators, to serve as report writers to gather information for research purposes on an ongoing basis. The investigators on this project will conduct the research studies and analysis necessary to answer the research questions. The investigators are clinicians with normal access to the medical records and each has their own individual medical record log in password.

The research is planned to continue indefinitely.

By reviewing the medical record information in this research, we will be able to, among other areas, study past trends, review treatment strategies, identiify adverse events and follow disease progression. This will allow the investigators to learn more about the specific diseases and disorders that our Division deals with.

**2.6.1** **Will blood samples be obtained as part of this research study?**

* No

*If submitting a protocol for expedited review, it should be clear that the planned blood draws are within the parameters described here: http://www.hhs.gov/ohrp/policy/expedited98.html (see Expedited Research Category #2)

If **Yes**, address the frequency, volume per withdrawal, the total volume per visit, and the qualifications of the individual performing the procedure:

## Study Flow Chart:

| Name | Modified Date |
|---|---|

[reviewer notes¬]

**2.7** **Will follow-up procedures be performed specifically for research purposes? Follow-up procedures may include phone calls, interviews, biomedical tests or other monitoring procedures.**

* No

[reviewer notes¬]

**2.8** **Does this research study involve the use of any questionnaires, interview or survey instruments?**

* No

## Upload a copy of all materials except for the SCID or KSADS which are on file at the IRB. The use of all instruments must be addressed in question 2.6 and/or question 2.7

**(except for an exempt submission where they should be addressed on the appropriate uploaded exempt form).**

| Name | Modified Date |
|---|---|

**Previously the name and publisher for commercially available materials were listed in the textbox below but effective 9/1/2015, all materials (except for the SCID and KSADS) must be uploaded using the Add button above.**

[reviewer notes¬]

**2.9** **If subjects are also patients, will any clinical procedures that are being used for their conventional medical care also be used for research purposes?**

* no

If **Yes,** describe the clinical procedures (and, if applicable, their frequency) that will be used for research purposes:

**2.10** The blood sample question was moved to 2.6.1.

[reviewer notes¬]

**2.11** **What is the total duration of the subject's participation in this research study across all visits, including follow-up surveillance?**

* N/A

[reviewer notes¬]

**2.12** **Does this research study involve any type of planned deception?**
If Yes, you are required to request an alteration of the informed consent process (question 4.7)

* No

**2.12.1** **Describe the planned deception:**

*

**2.12.2** **Provide a justification for this planned deception:**

*

**2.12.3** **Describe when and how subjects will be debriefed:**

*

[reviewer notes¬]

**2.13** **Does this research study involve the use of UPMC/Pitt protected health informationthat will be de-identified by an IRB approved "honest broker" system?**

* No

## 2.13.1 Identify the name of the honest broker system:

## 2.13.2 Specify the IRB-assigned honest broker system number (e.g., HB123456):

## 2.13.3 Specify the names of the individuals who will provide the honest broker services:

| Last | First | Organization |
|---|---|---|

There are no items to display

## Previous inputted information for Question 2.13.3:

## 2.13.4 Upload the signed honest broker assurance agreement:

| Name | Modified Date |
|---|---|

There are no items to display

[reviewer notes¬]

**2.14** **Will protected health information from a UPMC/Pitt HIPAA covered entity be accessed for research purposes or will research data be placed in the UPMC/Pitt medical record?**

* Yes

If you answer **Yes**, you are required to submit this study to the Research Informatics Office, Health Record Research Request (R3). Per UPMC Policy HS-RS0005, all research projects that access or involve UPMC electronic protected health information (e-PHI) must be submitted to R3, with the exception of clinical trials that are contracted through the UPMC Office of Sponsored Programs and Research Support (OSPARS).

Complete the R3 intake form available at http://rio.pitt.edu/services. An R3 representative will conduct a review. You will be notified once your R3 review is complete or if anything further is needed.

**Describe the medical record information that will be collected from the UPMC/Pitt HIPAA covered entity and/or the research-derived information that will be placed in the medical records.**

PHI will be obtained for research purposes but no data resulting from this research will be placed into a medical record. PHI will include medical history, diagnoses, demographics, vitals, and any information relevant to liver disease and or liver disorders, such as medications, laboratory and diagnostic test results, related co-morbid conditions and related surgical procedures.

**2.14.1** **Will protected health information from a non-UPMC/Pitt HIPAA covered entity be obtained for research purposes or will research data be placed in the non-UPMC/Pitt medical record?**

* No

**If Yes, describe how the HIPAA requirements will be met:**

**I,** Michael Dunn **, certify that any member of my research team accessing, reviewing and/or recording information from medical records have completed the CITI Privacy & Information Security course or, if completed within the past year, the Internet-Based Studies in Education and Research (ISER) HIPAA for Researchers (Formerly RPF Module 6). The HIPAA certificates must be available for review if audited but do not need to be uploaded into this OSIRIS application.**

* Yes

**2.14.2** **Are you requesting a waiver of the requirement to obtain written HIPAA authorization for the collection of the PHI?**

* Yes

[reviewer notes¬]

**2.14.2.1** **To ensure that this research use of the PHI involves no greater than minimal risk to privacy, describe your plan to protect patient-subject identifiers from improper use or disclosure.** [45 CFR 164.512 (i)(2)(ii)(A)(1)]

The protected health information collected for the purpose of this research study will ultimately have any obvious patient identifiers (e.g., name) removed from this information. The de-identified health information will be stored in a secure manner (e.g., password protected server/database) accessible only to the research study investigators and staff who are also involved in the health care of the respective patients. A study code linking the de-identified data with the identifiers will be maintained separately for all reviews. All information is accessed and maintained through password-protected UPMC servers, behind the secure UPMC firewalls, via physicians and staff who have completed HIPAA training, preventing improper use or disclosure.

A Request for Access to Decedent PHI has been submitted to UPMC for deceased individuals that may be included, and a signed form for this is attached under "Other Attachments".

**2.14.2.2 Describe your plan to destroy patient-subject identifiers at the earliest opportunity consistent with the research. Indicate at what point in the research those identifiers will be destroyed. If applicable, provide a health, research or legal justification for retaining the identifiers.** [45 CFR 164.512 (i)(2)(ii)(A)(2)]

De-identified data will be stored. A link connecting the de-identified data to patient identifiers will be maintained separately for research reasons so that if additional information is needed to achieve the goals of the study, it will be able to be gathered.

As this study is used to identify ongoing and historical disease and treatment trends, this link may be maintained indefinitely if necessary to meet the objectives of the study.

**2.14.2.3 Provide your assurance that this information will not be reused or disclosed to any other person or entity (i.e., other than the listed investigators and their research staff), except as required by law, for authorized oversight of the research study, or for other research for which the IRB has granted a waiver of the written HIPAA authorization.** [45 CFR 164.512 (i)(2)(ii)(A)(3)]

The information collected will only be shared among the investigators/staff/report writers involved with this study. Identifiable information will not be distributed outside of this project. If any data are shared with other investigators conducting similar research, it will be shared without identifiers and all appropriate data agreements will be executed. When possible, the sharing of dates and zip codes will be avoided. However, if dates and/or zip codes must be shared for scientific reasons, a limited data set with the appropriate data use agreement will be executed. Data will not be shared with any national or multicenter database or registry.

**2.14.2.4 Why could this research not practicably be conducted unless the waiver of written HIPAA authorization is granted?** [45 CFR 164.512 (i)(2)(ii)(B)]

Medical record information for clinical reasons is often available after a patient has left the hospital/office in which the information is collected. The physicians do not always know in advance who will have certain tests or information collected that would be relevant for this research. Without the waiver of written HIPAA authorization, the research could not be performed.

The sample size required is so large that including only those records/data for which consent can be obtained would prohibit conclusions to be drawn or bias the data such that conclusions would be skewed.

Many subjects for whom records would be reviewed are no longer followed and may be lost to follow-up. The proportion of individuals likely to have relocated or died is a significant percentage of the subject population and the research results may not be meaningful and lose statistical power.

**2.14.2.5 Why could this research not practicably be conducted without access to and use of the identifiable medical record information?** [45 CFR 164.512 (i)(2)(ii)(C)]

The overall scientific design of this study focuses on identifying and/or evaluating interrelationships among various medical variables that could not be accomplished without access to the PHI of the medical record. To link the information analyzed back to an individual and connect it with their medical history if additional information is required to answer the goals of this study, identifiable information is required. Consistant with the "minimum necessary standard" of the HIPPA privacy rule, we will access and collect only the information necessary to complete the research study.

**2.14.2.6** **Explain why the nature and amount of the medical record information that will be collected is felt to be the minimum necessary in order to conduct this research study.** [45 CFR 164.514 (d)]

For clinical purposes, the physician investigators have access to medical record information from the individuals who they wish to study. For the purposes of this research, the information that will be studied will only be what is needed to answer our research questions.

[reviewer notes¬]

**2.15** **Does this research study involve the long-term storage (banking) of biological specimens?**

* No

**2.15.1** **Broadly describe the intended future use of the banked biological specimens:**

**2.15.2** **Indicate the planned length of storage of the banked biological specimens:**

*

**2.15.3** **Will biological specimens be stored without identifiers or linkage codes?**

*

[reviewer notes¬]

**2.16** **Will research participants be asked to provide information about their family members or acquaintances?**

* No

**2.16.1** **Describe what information about the third party will be obtained from the participant:**

**2.16.2** **If the information about the third party is of a private nature, can the identity of the third party be readily ascertained or associated with this information?**

*

Describe the **private information** that will be collected and recorded about the third party:

[reviewer notes¬]

**2.17** **What are the main outcome variables that will be evaluated in this study?**

1. Survival
2. Improvement or progression of key complications such as gastrointestinal bleeding, fluid overload and encephalopathy
3. Development of co-morbid conditions such as cardiovascular disease in persons with nonalcoholic fatty liver disease
4. Need for interventions such as endoscopic banding of varices, paracentesis or liver transplantation

**2.18** **Describe the statistical approaches that will be used to analyze the study data.**

* Addressed below:

We will primarily rely on receiver operating characteristic (ROC) analyses to assess predictive value of clinical variable on specific outcomes. We will perform logistic regression analysis to assess potential covariate effects of multiple variables on the same outcome. Methodology will employ standard open source statistical analysis software packages.

[reviewer notes¬]

**2.19** **Will this research be conducted in (a) a foreign country and/or (b) at a site (e.g., Navajo Nation) where the cultural background of the subject population differs substantially from that of Pittsburgh and its surrounding communities?**

* No

Note that copies of training records, licenses, certificates should be maintained in the study regulatory binder and are subject to audit by the Research Conduct and Compliance Office (RCCO).

In addition, individuals planning to conduct human subject research outside the United States must complete an optional module on the CITI training website: International Studies. Click here to access the instruction sheet for accessing optional CITI modules.

**2.19.1** **Address the following for <u>each</u> of the foreign/culturally different sites where this research will be conducted:**

â€¢ Name of site
â€¢ Name of authorized individual (e.g., IRB Chair) from the local IRB or other human subject protections entity that is responsible for the review and approval of the project; upload approval letter with an English translation, if applicable

â€¢ Name and qualifications of the site collaborator responsible for the conduct of the research (e.g., site PI)
â€¢ The anticipated number of subjects that will be enrolled at that site
â€¢ If Federally funded, provide the Federalwide Assurance number (FWA) assigned to the site

*

| Site | Date Modified |
| --- | --- |
| There are no items to display | |

**2.19.1.1 Provide a description of the context of cultural norms and local laws and highlight differences between U.S. culture in all areas relevant to your study, including, at a minimum:**

â€¢ Age of majority of participants to be enrolled
â€¢ If study includes minors or decisionally impaired subjects, summarize laws on guardianship
â€¢ If your study involves any invasive medical procedure (including blood draws), provide assurance that the individuals undertaking those procedures for research purposes are appropriately credentialed.
â€¢ If your study involves the administration of a drug, device or biologic for research purposes, describe the process for shipping, labeling, storing and dispensing, and indicate how these are consistent with all relevant local (and US) laws, including those requiring import / export permits.
â€¢ If your study involves collection of biological specimens, describe the process for shipping, labeling, storing and using such samples. Identify any special local consent requirements, and any special permits that may be required by local law.

*

**2.19.1.2 Describe any aspects of the local cultural, political or economic climate that might increase the risks of harm for either local participants or researchers. Describe the steps you will take to minimize these risks. UPitt Faculty, Staff, and Students must access the Travel Registry page. Go to my.pitt.edu and the link is displayed under My Resources.**

*

**2.19.2 Will all individuals being recruited to participate in this research study be able to read and comprehend English**

*

If **No**, describe how consent will be obtained. Explain provisions for culturally appropriate recruitment and consent accommodations such as, translations or involvement of native language speakers, especially if literacy is not widespread in this country.

**2.19.2.1** **If translated documents are used, upload a signed translator certification form and back translations (if applicable):**
(Translator Certification Form is available under the ***Resources*** tab located to right of this item)

| Name | Modified Date |
|---|---|
| There are no items to display | |

**2.19.3** **Will all of the research procedures described in this IRB application be conducted at the foreign/culturally different sites?**

* ( )( )Yes ( )( )No

If **No**, describe the subset of research procedures to be performed at the sites:

**2.19.4** **To what extent do the local site requirements to protect subject confidentiality and privacy differ from US standards. If applicable, explain how those will be addressed by this research team:**

*

**2.19.5** **If the researcher is a student, describe how the student will communicate with the advisor during the conduct of the research and how the advisor will oversee the research:**

[reviewer notes¬]

**2.21** **Will this research study be conducted within a nursing home located in Pennsylvania?**

* No

**2.21.1** **Does this research involve a medical procedure or an experimental treatment?**

*

**2.21.2 Does the research study involve the exposure of nursing home residents to pain, injury, invasion of privacy, or ask the resident to surrender autonomy?**

*

If **Yes to either question**, upload the Pennsylvania Department of Health approval letter.
28 PA Code Section 201.29 (o) specifies that prior to the initiation of research, and in addition to IRB approval, any study that includes experimental research or treatment conducted in a nursing home must be approved by the Pennsylvania Department of Health. A signed consent form from nursing home resident-subject is also required.

| Name | Modified Date |
|---|---|

Section: Section 3 - Human Subjects

[reviewer notes¬]

## Section 3 - Human Subjects

**3.1 What is the age range of the subject population?**

greater than or equal to 18 years of age

**3.2 What is their gender?**

* Both males and females

Provide a justification if single gender selected:

**3.3 Will any racial or ethnic subgroups be explicitly excluded from participation?**

* No

If **Yes**, identify subgroups and provide a justification:

**3.4 For studies conducted in the U.S., do you expect that all subjects will be able to comprehend English?**

* Yes

If **No**, identify what languages will be understood by subjects and describe your plan to manage communication with non-English speaking subjects during all phases of the study:

**3.4.1** **If translated documents are used, upload a signed translator certification form and back translations (if applicable):**

| Name | Modified Date |
|---|---|
| There are no items to display | |

[reviewer notes¬]

**3.5** **<u>Participation of Children</u>: Will children less than 18 years of age be studied?**

* No

If **No**, provide a justification for excluding children:
Children under the age of 18 are not treated in our clinic

**3.5.1** **Specify the age range of the children to be studied.**
(Check all that apply below:)

*

| Choices |
|---|
| There are no items to display |

**3.5.2** **Provide a rationale for the specific age ranges of the children to be studied:**

**3.5.3** **Describe the expertise of the study team for conducting research with children within this age range:**

**3.5.3.1** **Have you obtained the following clearances from all research staff who may have direct contact with children under the age of 18? Direct contact under the law includes face-to-face, and telephonic or electronic, contact with minors. Please see the<u>Child Clearances</u> guidance document for further explanation?**

**Pennsylvania Department of Public Welfare Child Abuse History Clearance;**
**Pennsylvania State Police Criminal Record Check; and**
**FBI Criminal Background Check**

**Note:** If No, once all clearances are obtained, a modification must be submitted.

**If you selected N/A, please explain:**

It is important to note that â€œdirect contactâ€□ refers not only to face-to-face meetings but also extends to communication via phone (including text messaging), social media or internet. Direct contact also includes the care, guidance, supervision or control, or routine interaction with, minors. Conversely, a participating investigator or support staff member who does not have direct contact, either electronically or in person, with children does not need to obtain clearances (e.g., statistician, non-clinical laboratory personnel, etc.). If your research study provides babysitting services, the babysitters must have the required child clearances.

* **Note:** It is the **responsibility of the principal investigator** to ensure that all research staff have these clearances prior to any interaction with children. Contact Human Resources at 412-624-8150 for assistance with this process.

3.5.4 **Describe the adequacy of the research facilities to accommodate children within this age range:***

3.5.5 **Permitted Categories of Research: The Federal Policy and FDA regulations governing human subject protections specify that research involving children must fall into one of the following permitted categories.**

*

## 45 CFR 46.406

- The risk represents only a minor increase over minimal risk.
- The research procedures present experiences to the subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.
- The research procedures are likely to yield generalizable knowledge about the subjectsâ€™ disorder or condition which is of vital importance for understanding or amelioration of the subjectsâ€™ disorder or condition.

## 45 CFR 46.407

- The risk is justified by the anticipated benefit to the subjects; and the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

Provide a justification which **must address all considerations** related to the designated category of research:

[reviewer notes¬]

**3.6** **Does this research study involve prisoners, or is it anticipated that the research study may involve prisoners?**

***** No

**3.6.1** **The Federal Policy and FDA regulations specify that research involving prisoners must fall into one of the following permitted categories.**

*

*Provide a justification for your designation:

**General Requirements**: The Federal Policy and FDA regulations specify that research involving prisoners must also conform to each of the following general requirements. Describe how your study **meets each of the following regulations**.

**3.6.2** **Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in the prison are not of such a magnitude that the prisonerâ€™s ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.** ***[45 CFR 46.305 (a)(2)]***
*

**3.6.3** **The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers.**
***[45 CFR 46.305 (a)(3)]***
*

**3.6.4** **The procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners.**
***[45 CFR 46.305 (a)(4)]***
*

**3.6.5** **Information regarding the research is presented to the potential prisoners-subjects in a language which is understandable to them.*****[45 CFR 46.305 (a)(5)]***

*

**3.6.6** **Adequate assurance exists that the parole boards will not take into account a prisonerâ€™s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.** ***[45 CFR 46.305 (a)(6)]***

*

**3.6.7** **Where there may be a need for follow-up examination or care of the prisoners-subjects after the end of their participation in the research, adequate provision has been made for such examination or care; taking into account the varying lengths of individual prisonersâ€™ sentences, and the prisoners have been informed of this fact.** ***[45 CFR 46.305 (a)(7)].***

*

[reviewer notes¬]

**3.7** **Will pregnant women be knowingly and purposely included in this research study?**

* No

**General Requirements**: The Federal Policy **[45 CFR 46, Subpart B]** specify that research involving pregnant women and/or fetuses must also confirm to each of the following criteria. Describe how your study meets each of the requirements.

**3.7.1** **Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.** ***[45 CFR 46.204 (a)]*** [Include references]

*

**3.7.2** **The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the women or the fetus; or, if there is no such prospect of direct benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.** ***[45 CFR 46.204 (b)]***

*

**3.7.3** **Any risk is the least possible for achieving the objectives of the research.** ***[45 CFR 46.204 (c)]***

*

**3.7.4** **No inducements, monetary or otherwise, will be offered to terminate the pregnancy.** ***[45 CFR 46.204 (h)]***

*

**3.7.5** **Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.** ***[45 CFR 46.204 (i)]***

*

**3.7.6** **Individuals engaged in the research will have no part in determining the viability of a neonate.** ***[45 CFR 46.204 (j)]***

*

[reviewer notes¬]

**3.8** **Does this research study involve neonates of uncertain viability or nonviable neonates?**

* No

General Requirements: The Federal regulations **[45 CFR 46.205]** specify that research involving neonates of uncertain viability and nonviable neonates must conform to each of the general requirements. Describe how each of the following requirements will be met.

**3.8.1** **Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates (include references).** *[45 CFR 46.205 (a)(1)]*

*

**3.8.2** **Individuals engaged in the research will have no part in determining the viability of the neonate.** *[45 CFR 46.205 (a)(3)]*

*

**3.8.3** **Does this research study involve neonates of uncertain viability?** [45 CFR 46.205(b)]

*

**3.8.3.1** **The Federal regulations specify that, until it is ascertained whether or not a neonate is viable, a neonate may <u>not</u> be involved in research unless one of the following conditions is met.**

*

*Provide a justification for your selection:

**3.8.4** **Does this research study involve nonviable neonates?** [45 CFR 46.205(c)]

*

General Requirements: The Federal regulations specify that, after delivery, a nonviable neonate may not be involved in research unless each of the following additional conditions are met [**45 CFR 46.205(c)**].

**3.8.4.1** **Vital functions of the neonate will not be artificially maintained.** *[45 CFR 46.205 (c)(1)]*

*

**3.8.4.2** **The research will not terminate the heartbeat or respiration of the neonate.** *[45 CFR 46.205 (c)(2)]*

*

**3.8.4.3** **There will be no added risks to the neonate resulting from the research.** *[45 CFR 46.205 (c)(3)]*

*

**3.8.4.4** **The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.** *[45 CFR 46.205 (c)(4)]*

*

[reviewer notes¬]

**3.9** **Fetal Tissues: Does this research involve the use of fetal tissues or organs?**

* No

General Requirements: In accordance with the Pennsylvania Abortion Control Act, fetal tissues or organs may only be obtained for use in research subsequent to obtaining the written informed consent of the mother. The Pennsylvania Abortion Control Act specifies that research involving the use of fetal tissue or organs must also conform to **each** of the following requirements. [Indicate how you will conform to each requirement]

**3.9.1** **Informed consent for the research use of fetal tissue derived from an abortion will be obtained separate from, and after, the decision and consent to abort has been made.**

*

**3.9.2** **No consideration of any kind (i.e., monetary or otherwise) will be offered to the mother in obtaining her consent for the research use of the fetal tissue or organs.**

*

**3.9.3** **The mother will not be permitted to designate a recipient of the fetal tissue or organs for use in research.**

*

**3.9.4** **All persons who participate in the procurement or use of the fetal tissue or organs will be informed as to the source of the tissue (e.g., abortion, miscarriage, stillbirth, ectopic pregnancy).**

*

[reviewer notes¬]

**3.10** **What is the total number of subjects to be studied at this site, including subjects to be screened for eligibility?**

Note: The number below is calculated by summing the data entered in question 3.11. Any additions or changes to the values entered in 3.11 will be reflected in 3.10.

--
->

* 200000

**3.11** **Identify each of the disease or condition specific subgroups (include healthy volunteers, if applicable) that will be studied.**

**Click on the "Add" button and specify for <u>each</u> subgroup:**

**1) how many subjects will undergo research related procedures at this site; and**

**2) if applicable, how many subjects will be required to undergo screening procedures (e.g., blood work, EKG, x-rays, etc.) to establish eligibility. Do Not include subjects who will undergo <u>preliminary telephone screening</u>.**

*

| | Subgroup | Number to undergo research procedures | Number to undergo screening procedures |
|---|---|---|---|
| View | Patients with liver disease | 200000 | 0 |

**3.12** **Provide a statistical justification for the total number of subjects to be enrolled into this research study at the multicenter sites or this site.**

* Described below:

We are estimating the number of subjects based on 5,000 new patients seen annually for the next 20 years as well as a timespan of the past 20 years for recorded electronic record information.

[reviewer notes¬]

**3.13** **Inclusion Criteria: List the specific criteria for inclusion of potential subjects.**

All patients with liver disease 18 years of age and older.

**3.14** **Exclusion Criteria: List the specific criteria for exclusion of potential subjects from participation.**

N/A

**3.15** **Will HIV serostatus be evaluated specifically for the purpose of participation in this research study?**

* No

If **Yes**, provide a justification:

Section: Section 4 - Recruitment and Informed Consent Procedures

[reviewer notes¬]

**4.1** Select all recruitment methods to be used to identify potential subjects:
Not applicable, no subject interaction will occur

## Advertisements

Upload the advertisements for review:

Name Modified Date

## Honest Broker

Identify the name of the honest broker system and name of the specific individuals who will provide those services:

Specify the IRB-assigned honest broker system number (e.g., HB123456):

Upload the signed honest broker assurance agreement:

Name Modified Date

There are no items to display

## Recruitment Letters and Scripts

Upload recruitment letters/scripts/text:

Name Modified Date

**Research Registry**

List the IRB approval number and title for each registry source:

**4.2** **Provide a detailed description of your recruitment methods, including identifying and initiating contact with participants:**

This research involves all patients in the Center for Liver Diseases and the Starzl Transplant Institute and no interaction with subjects will occur.

Note: Questions jump from 4.2 to 4.6 as questions 4.3-4.5 have been removed and the information is now captured in 4.1

[reviewer notes¬]

**4.6** **Are you requesting a waiver to document informed consent for any or all participants, for any or all procedures? (e.g., a verbal or computerized consent script will be used, but the subjects will not be required to sign a written informed consent document.** ***This is not a waiver to obtain consent.***

* No

**4.6.1** **Identify the specific research procedures and/or the specific subject populations for which you are requesting a waiver of the requirement to obtain a signed consent form.**

**If not all**, identify the specific procedures and/or subject populations for which you are requesting a waiver:

**4.6.2** **Indicate which of the following regulatory criteria is applicable to your request for a waiver of the requirement to obtain a signed consent form.**

**45 CFR 46.117(c)(1)** That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

**45 CFR 46.117(c)(2)** That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

**4.6.2.1** **Address why the specific research procedures for which you are requesting a waiver of the requirement to obtain a signed consent form present no more than minimal risk of harm to the research subjects:**

**4.6.2.2** **Justify why the research listed in 4.6.1 involves no procedures for which written informed consent is normally required outside of the research context:**

**4.6.3** **Address the procedures that will be used and the information that will be provided (i.e., script) in obtaining and documenting the subjects' verbal informed consent for study participation:**

Upload Scripts:
Name Modified Date

[reviewer notes¬]

**4.7** **Are you requesting a waiver to obtain informed consent or an alteration of the informed consent process for any of the following?**

* Yes

**4.7.1** **If Yes, select the reason(s) for your request:**
Review of identifiable medical records and/or specimens

General Requirements: The Federal Policy **[45 CFR 46.116 (d)]** specifies in order for a waiver of consent to be approved, the request must meet four criteria. For each request, you will be asked to provide a justification addressing how each of these criterion is met.

**Medical record review for the identification of potential subjects:**

The research involves no more than minimal risk to the subjects;
**[45 CFR 46.116 (d)(1)]**
The waiver or alteration will not adversely affect the rights and welfare of the subjects;
**[45 CFR 46.116 (d)(2)]**

The research could not practicably be carried out without the waiver or alteration;
**[45 CFR 46.116 (d)(3)]**
Whenever appropriate, the subjects will be provided with additional pertinent information after participation;
**[45 CFR 46.116 (d)(4)]**

**Review of identifiable medical records:** [Note: A waiver of HIPAA Authorization must be requested (2.14.2)] **Include the approximate number of medical records and/or specimens that will be accessed and enter -1 in question 3.11 for the number of subjects to be enrolled.**

| | |
|---|---|
| The research involves no more than minimal risk to the subjects;<br>**[45 CFR 46.116 (d)(1)]** | This project involves retrospective and prospective collection of medical record information. All of the data being used for this project contain information to which the investigators already have clinical access. The only foreseeable risk is breach of confidentiality, as can occur with any research, and we will make all efforts to secure information used for research. A request for Access to Decedent PHI has been submitted to UPMC for deceased individuals that may be included, and a signed form for this is attached under"Other Attachments". |
| The waiver or alteration will not adversely affect the rights and welfare of the subjects;<br>**[45 CFR 46.116 (d)(2)]** | The investigators of this research have access to medical record information for clinical purposes. The information being used for research is already available to the physician researchers and will not adversely affect the rights and welfare of the subjects |
| The research could not practicably be carried out without the waiver or alteration;<br>**[45 CFR 46.116 (d)(3)]** | Medical record information for clinical reasons is often available after a patient has left the hospital/office in which the information is collected. The physicians do not always know in advance who will have certain tests or information collected that would be relevant for this research. Without the waiver of consent, the research could not be performed.<br><br>The sample size required is so large that including only those records/data for which consent can be obtained would prohibit conclusions to be drawn or bias the data such that conclusions would be skewed.<br><br>Many subjects for whom records would be reviewed are no longer followed and may be lost to follow-up. The proportion of individuals likely to have relocated or died is a significant percentage of the subject population and the research results may not be meaningful and lose statistical power. |

| | |
|---|---|
| Whenever appropriate, the subjects will be provided with additional pertinent information after participation. **[45 CFR 46.116 (d)(4)]** | The results of this research will not be relevant to individual clinical use for specific subjects, however, if for any reason additional pertinent information is relevant to patients, it will be shared with them. |

## Parental Permission and/or Child Assent

The research involves no more than minimal risk to the subjects;
**[45 CFR 46.116 (d)(1)]**
The waiver or alteration will not adversely affect the rights and welfare of the subjects;
**[45 CFR 46.116 (d)(2)]**
The research could not practicably be carried out without the waiver or alteration;
**[45 CFR 46.116 (d)(3)]**
Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
**[45 CFR 46.116 (d)(4)]**

## Alteration of informed consent process

The research involves no more than minimal risk to the subjects;
**[45 CFR 46.116 (d)(1)]**
The waiver or alteration will not adversely affect the rights and welfare of the subjects;
**[45 CFR 46.116 (d)(2)]**
The research could not practicably be carried out without the waiver or alteration;
**[45 CFR 46.116 (d)(3)]**
aWhenever appropriate, the subjects will be provided with additional pertinent information after participation.
**[45 CFR 46.116 (d)(4)].**

## Other Minimal Risk activity

The research involves no more than minimal risk to the subjects;
**[45 CFR 46.116 (d)(1)]**
The waiver or alteration will not adversely affect the rights and welfare of the subjects;
**[45 CFR 46.116 (d)(2)]**
The research could not practicably be carried out without the waiver or alteration;
**[45 CFR 46.116 (d)(3)]**
Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
**[45 CFR 46.116 (d)(4)].**

**4.7.2** **Under what circumstances (if any) will you obtain consent from some of these subjects?**

None

[reviewer notes¬]

**4.8** **Are you requesting an exception to the requirement to obtain informed consent for research involving the evaluation of an 'emergency' procedure?**

**Note:** This exception allows research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent.

* No

[reviewer notes¬]

**4.9** **Upload all consent documents for watermarking:**

Draft Consent Forms for editing:

Name Modified Date

Approved Consent Form(s):

Name Modified Date

[reviewer notes¬]

**4.10** **Will all potential adult subjects be capable of providing direct consent for study participation?**

*
Not applicable

**Indicate why direct consent is not possible:**
This is a retrospective and prospective analysis with a request for waiver of HIPPA Authorization and waiver of consent

**4.10.1** **Provide a justification for the inclusion of adult subjects who are unable to provide direct consent for study participation.**

**4.10.2** **Specify the criteria used to determine that a potential adult subject is not able to provide direct consent for participation and identify who will be responsible for that determination.**

**4.10.3** **Will you obtain the potential adult subject's assent for study participation?**

*

If **No**, provide a justification for not obtaining assent:

**4.10.4** **Identify who will provide proxy consent for the participation of the decisionally impaired adult:**

[reviewer notes¬]

**4.11** **At what point will you obtain the informed consent of potential research subjects or their authorized representative?**

Other - describe below

If **Other**, address below:
This is a retrospective and prospective analysis with a request for waiver of HIPPA Authorization and waiver of consent

**4.11.1** **Address why you feel that it is acceptable to defer obtaining written informed consent until after the screening procedures have been performed.**

**4.11.2** **Taking into account the nature of the study and subject population, indicate how the research team will ensure that subjects have sufficient time to decide whether to participate in this study. In addition, describe the steps that will be taken to minimize the possibility of coercion or undue influence.**

This is a retrospective and prospective analysis with a request for waiver of HIPPA Authorization and waiver of consent

[reviewer notes¬]

**4.12** **Describe the process that you will employ to ensure the subjects are fully informed about this research study.**

* Not applicable; see previous request for a waiver of informed consent for all aspects of this research study (question 4.7)

**This description must include the following elements:**

- who from the research team will be involved in the consent process (both the discussion and documentation);
- person who will provide consent or permission;
- information communicated; and
- any waiting period between informing the prospective participant about the study and obtaining consent

In addition, address the following if applicable based on your subject population:

- process for child assent and parental permission
  - continued participation if a child subject turns 18 during participation
- process for obtaining proxy consent and assent for decisionally impaired subjects
  - continued participation if subject regains capacity to consent

**4.13** **Are you requesting an exception to either IRB policy related to the informed consent process?**

- For studies involving a drug, device or surgical procedures, a *licensed physician who is a listed investigator* is required to obtain the written informed consent unless an exception to this policy has been approved by the IRB
- For all other studies, a *listed* investigator is required to obtain consent (Note: In order to request an exception to this policy, the study must be minimal risk)

* No

If **Yes**, provide a justification and describe the qualifications of the individual who will obtain consent:

**4.14** **Will you inform research subjects about the outcome of this research study following its completion?**

* No

If **Yes**, describe the process to inform subjects of the results:

Section: Section 5 - Potential Risks and Benefits

[reviewer notes¬]

**5.1** **Describe potential risks (physical, psychological, social, legal, economic or other) associated with screening**

**procedures, research interventions/interactions, and follow-up/monitoring procedures performed specifically for this study:**

*

View

| | |
|---|---|
| **Research Activity:** | Collection of clinical information for research use |
| **Common Risks:** | *No Value Entered* |
| **Infrequent Risks:** | *No Value Entered* |
| **Other Risks:** | There is a rare risk for breach of confidentiality |

**5.1.1** **Describe the steps that will be taken to prevent or to minimize the severity of the potential risks:**

The physicians involved with this research have clinical responsibilities and understand the importance of privacy and confidentiality. Data will be kept secure within the Department and when analyzed in spreadsheets, will be de-identified. Data will be stored behind the UPMC firewall and password-protected.

**5.2** **What steps will be taken in the event that a clinically significant, unexpected disease or condition is identified during the conduct of the study?**

* **Not Applicable**

**5.3** All the risk questions (screening, intervention/interaction, follow-up) have been merged into one question (5.1).

[reviewer notes¬]

**5.4** **Do any of the research procedures pose a physical or clinically significant psychological risk to women who are or may be pregnant or to a fetus?**

* No

**5.4.1** **List the research procedures that pose a risk to pregnant women or fetuses:**

**5.4.2** **Describe the steps that will be taken to rule out pregnancy prior to exposing women of child-bearing potential to the research procedures that pose a risk to pregnant women or fetuses:**

**5.4.3** **Describe the measures to prevent pregnancy, and their required duration of use, that will be discussed with women of child-bearing potential during and following exposure to research procedures:**

[reviewer notes¬]

**5.5** **Do any of the research procedures pose a potential risk of causing genetic mutations that could lead to birth defects?**

* No

**5.5.1** **List the research procedures that pose a potential risk of genetic mutations/birth defects:**

**5.5.2** **Describe the measures to prevent pregnancy, and their required duration of use, in female subjects and female partners of male subjects during and following exposure to research procedures:**

[reviewer notes¬]

**5.6** **Are there any alternative procedures or courses of treatment which may be of benefit to the subject if they choose not to participate in this study?**

* Not applicable

If **Yes**, describe in detail:

[reviewer notes¬]

**5.7** **Describe the specific endpoints (e.g., adverse reactions/events, failure to demonstrate effectiveness, disease progression) or other circumstances (e.g., subject's failure to follow study procedures) that will result in discontinuing a subjectâ€™s participation?**

* Not applicable - There are no anticipated circumstances that would lead to discontinuing a subjectâ€™s participation in this research study.

[reviewer notes¬]

**5.8** **Will any individuals other than the investigators/research staff involved in the conduct of this research study and authorized representatives of the University Research Conduct and Compliance Office (RCCO) be permitted access to research data/documents (including medical record information) associated with the conduct of this research study?**

* Yes

**5.8.1** **Identify the 'external' persons or entity who may have access to research data/documents and the purpose of this access:**

If any data are shared with other investigators conducting similar research, it will only be shared without identifers and the appropriate data agreements will be executed. When possible, the sharing of dates and/or zip codes will be avoided. However, if dates and/or zip codes must be shared for scientific reasons, a limited data set with the appropriate data use agreement will be executed. Data will not be shared with any national or multicenter database or registry.

**5.8.2** **Will these 'external' persons or entity have access to identifiable research data/documents?**

*

No; the research data/documents will be coded and subject identifiers removed prior to access by the external persons

If **Yes**, describe how they will protect the confidentiality of the research data:

**5.9** **Has or will a Federal Certificate of Confidentiality be obtained for this research study?**

* No

**5.10** **Question has been moved to 5.17**

**5.11** **Question has been moved to 5.16**

[reviewer notes¬]

**5.12** **Does participation in this research study offer the potential for direct benefitto the research subjects?**

No - Describe the general benefits to society (e.g., increased knowledge; improved safety; better health; technological advancement) that may result from the conduct of this research study.

Describe the benefit:
This will result in increased knowledge of the various types of liver disease and how it impacts the patient. The investigator will be able to evaluate present methods and may be able to determine new methods for the treatment and cure of complex liver disease. We will review the electronic clinical records of patients seen in the Center for Liver Diseases and the Starzl Transplant Institute in order to discover how to use clinical information to diagnose and predict the outcome of complex liver diseases and their potential for cure or improvement with new forms of treatment.

**5.13 Describe the data and safety monitoring plan associated with this study. If the research study involves multiple sites, the plan must address both a local and central review process.**

The data and safety monitoring plan for the study will involve routine (i.e., semi-annual) monitoring by the Principal Investigator and coordinator of 1) the security of the databases within the UPMC clinical firewall; 2) any conditions that may negatively impact the confidentiality of information contained within the study.

The PI will be informed of, and review all requests for reviews conducted under this IRB submission to ensure that all meet the requirements and aims approved in this submission. The investigator of any review being conducted wil inform the PI of any issues or breaches of confidentiality. This information will be included in the semi-annual data and safety monitoring review.

A summary report of the data and safety monitoring activities will be included in the annual renewal report to the IRB.

[reviewer notes¬]

## Section 5 - Potential Risks and Benefits of Study Participation

**5.14 What precautions will be used to ensure subject privacy is respected?** (e.g. the research intervention will be conducted in a private room; the collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected, drapes or other barriers will be used for subjects who are required to disrobe)

This is a retrospective and prospective analysis with a request for waiver of HIPPA Authorization and a waiver of consent.

The collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research so that no unneeded sensitive information is being collected.

**5.15 What precautions will be used to maintain the confidentiality of identifiable information?** (e.g., paper-based records will be kept in a secure location and only be accessible to personnel involved in the study, computer-based files will only be made available to personnel involved in the study through the use of access

privileges and passwords, prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information, whenever feasible, identifiers will be removed from study-related information, precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys, audio and/or video recordings of subjects will be transcribed and then destroyed to eliminate audible identification of subjects)

All identifiable material/data will be kept secure within the department and will only be accessible to personnel involved with the research. Computer-based files will only remain available to personnel involved in the study through use of access privileges and passwords. All investigators and research personnel have completed research and HIPAA training and understand well the importance of maintaining confidentiality of research data. Stored data will be de-identified. A study code linking the de-identified data with the identifiers will be maintained for all reviews.

**5.16 If the subject withdraws from the study, describe what, if anything, will happen to the subjectâ€™s research data or biological specimens.**

N/A - This is a retrospective and prospective analysis with a request for waiver of HIPAA Authorization and waiver of consent.

**5.17 Following the required data retention period, describe the procedures utilized to protect subject confidentiality.** (e.g., destruction of research records; removal of identifiers; destruction of linkage code information; secured long-term retention)

All material and data will be securely maintained for an indefinite period of time in the Center for Liver Diseases and Starzl Transplant Institute.

Data will be stored without identifiers in a pass protected database. A separate study code linking the de-identified data with the identifiers will be maintained for all reviews.

Section: Section 6 - Costs and Payments

[reviewer notes¬]

**6.1 Will research subjects or their insurance providers be charged for any of the procedures (e.g., screening procedures, research procedures, follow-up procedures) performed for the purpose of this research study?** *

No

**6.1.1** **Specify what research procedures will be billed to the subject or insurance provider:**

**6.1.2** **Provide a justification for billing subjects or insurance providers for procedures that are performed solely for the purpose of the research study.**

**6.1.3** **Will subjects or insurance providers be billed for the investigational drug or device being evaluated or used in this research study?**

*

**Provide assurance that the FDA has given approval for the sponsor of this research study to charge investigators for the investigational drug or device.**

**If this is an investigational device, indicate if the Health Care Financing Administration has designated it as a Class B medical device.**

*

**6.1.4** **Address the contingencies that are in place to ensure that potential subjects, who may desire to participate in this research study but are not able to bear this personal financial risk, will be afforded access to study participation.**

[reviewer notes¬]

**6.2** **Will subjects be compensated in any way for their participation in this research study?**

* No

**6.2.1** **Describe the amount of payment or other remuneration offered for complete participation in this research study.**

**6.2.2** **Describe the amount and term of payment or other remuneration that will be provided for partial completion of this research study.**

Section: Section 7 - Qualifications and Source(s) of Support

[reviewer notes¬]

7.1

## Summarize the qualifications and expertise of the principal investigator and listed co-investigators to perform the procedures outlined in this research study.

Michael Dunn, MD is a Professor of Medicine in the Division of Gastroenterology, Hepatology and Nutrition. He has been a Principal Investigator as well as a Co-Investigator on multiple studies. He is an attending physician within the Center for Liver Diseases. He has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Kapil Chopra, MD is an Associate Professor of Medicine in the Division of Gastroenterology, Hepatology, and Nutrition. He has been an Investigator and Co-Investigator on multiple studies. He is an attending physician within the Center for Liver Diseases. He has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Mordechai Rabinovitz, MD is a Professor of Medicine in the Division of Gastroenterology, Hepatology, and Nutrition. He has been a Principal Investigator as well as a Co-Investigator on multiple studies. He is an attending physician within the Center for Liver Diseases. He has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Patricia Gironda is a certified nurse practitioner in the Division of Gastroenterology, Hepatology, and Nutrition, who is experienced in taking care of patients with liver problems and has several years of experience in research. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Jaideep Behari, MD is an assistant professor in the Division of Gastroenterology, Hepatology and Nutrition. He has been a Co-Investigator in multiple studies. He is an attending physician within the Center for Liver Diseases. He has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Obaid S Shaikh, MD is a Professor of Medicine in the Division of Gastroenterology, Hepatology and Nutrition. He has been a Principal Investigator as well as a Co-Investigator on multiple studies. He is an attending physician within the Center for Liver Diseases. He has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Amy Schmotzer, RN BSN is a registered nurse in the Division of Gastroenterology, Hepatology, Nutrition. She has been a registered nurse for 31 years with 18 years of experience in Research and several years of experience working with patients with liver disease. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Anita Lippello, CRNP, is a certified nurse practitioner in the Division of Gastroenterology, Hepatology, and Nutrition who is experienced in taking care of patients with liver problems and has several years of experience in research. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Shahid Malik MD is an assistant professor in the Division of Gastroenterology, Hepatology and Nutrition. He has multiple years of experience in Liver Disease and research. He is an attending physician within the Center for Liver Diseases. He has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Swaytha Ganesh, MD is a member of the CLD staff. She has multiple years of experience in Liver Disease and research. She is an attending physician within the Center for Liver Diseases. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Julia Greer, MD is an assistant professor in the Division of Gastroenterology, Hepatology and Nutrition. She has several years of experience in research and liver disease. She is a physician within the Center for Liver Diseases. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Mary Beth Luce, RN is a registered nurse in the Division of Gastroenterology, Hepatology, Nutrition. She has multiple years of experience in Research and working with patients with liver disease. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Christopher Hughes, MD is an Associate Professor of Surgery, specializing in liver surgery. He has been a Principal Investigator as well as a Co-Investigator on multiple studies. He has daily contact with CLD and STI patients and participates in their management.

Abhinav Humar, MD is a Professor of Surgery. He is the Clinical Director, Starzl Transplantation Institute Division Chief, Transplant Surgery, specializing in liver surgery. He has been a Principal Investigator as well as a Co-Investigator on multiple studies. He has daily contact with CLD and STI patients and participates in their management.

Alison Jazwinski, MD is a member of the CLD staff with several years of experience in Liver Disease and research. She is an attending physician within the Center for Liver Diseases. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Allan Tsung, MD is an Assistant Professor of Surgery, specializing in liver surgery. He has been a Principal Investigator as well as a Co-Investigator on multiple studies. He has daily contact with CLD and STI patients and participates in their management.

Amit Tevar, MD is surgeon within the Starzl Transplant Institute and has daily contact with CLD and STI patients and routinely participates in their management.

Anthony Demetris, MD, Starzl Professor of Liver and Transplant Pathology, is a faculty member at the University of Pittsburgh. He is the primary pathologist for patients in the CLD/STI. He has several years of experience in liver disease and research.

Vikrant Rachakonda, MD, is an attending physician within the Center for Liver Diseases and the Starzl Transplant Institute. He has several years of experience in liver disease and research.

Alessandro Furlan MD is a faculty member at the University of Pittsburgh. He is the primary abdominal radiologist for patients in the CLD/STI. His expertise is utilized by the CLD/STI attending staff on a routine basis for complex imaging issues on CLD/STI patients. He has several years of experience in liver imaging.

Margaret Andrzejewski PA-C is a certified Physician's Assistant in the Division of Gastroenterology, Hepatology, and Nutrition, who is experienced in taking care of patients with liver problems and has experience in research.

Andrea F. DiMartini, MD is an Associate Professor of Psychiatry and leads the Starzl Transplant Institute's transplant psychiatry program. She is an experienced clinical investigator who has published multiple studies on cirrhotic patients awaiting transplantation. She has daily contact with the patients in our clinic and participates in their management.

Jian-Min Yuan, MD, PhD. is a faculty member at the University of Pittsburgh. He is an expert in liver cancer and epidemiology. Liver cancer is a common endpoint of chronic liver diseases. His expertise is utilized by the CLD/STI attending staff on a routine basis.

Anjouli Dapice PA-C is a physician assistant working in the Center for Liver Diseases/Starzl Transplant Institute. She is working extensively with this patient population.

Dr. Ramon Bataller is a trained hepatologist and physician-scientist who has more than 20 years clinical experience, caring for patients with advanced liver disease. Dr. Batallerâ€™s main scientific interest are consequences of chronic liver injury,

and he has focused over the past 7 years on merging his clinical and scientific interests to investigate determinants of outcome in patients with chronic alcohol abuse. Dr. Bataller organized the 2008 EASL Monothematic Conference on Alcoholic Liver Disease, directed the AASLD Early Morning Workshop on Alcoholic Liver disease and contributed to the EASL Practical Clinical Guidelines on Alcoholic Liver Disease. Dr. Bataller is a former Associate Editor of Gut,and the author of 110 peer-reviewed PubMed listed papers, many of those in high impact such as JCI, Gastroenterology, Hepatology and Cancer Cell.

Nadia Jonassaint MD is an attending physician within the Center for Liver Diseases with several years of experience in Liver Disease and research. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Pamela Bloomer PT/MPT is a physical therapist working within the STI Liver Transplant clinic. She has extensive experience with patients with frailty and deconditioning.
Amy Manfredi RN BS is a registered nurse and the Nursing Director in the Starzl Transplant Institute / Center for Liver Diseases. She has multiple years of experience in Research and working with patients with liver disease. She has daily contact with patients in both the Center for Liver Diseases and the Starzl Transplant Institute.

Lisa Graham PA-C is a physician assistant working in the Center for Liver Diseases/Starzl Transplant Institute. She has multiple years of clinical and research experience. She is working extensively with this patient population.

Becky Donovan is a nurse working in the Center for Liver Diseases/Starzl Transplant Institute. She has multiple years of clinical and research experience. She is working extensively with this patient population.

[reviewer notes¬]

**7.2 Indicate all sources of support for this research study.**

*
Selections
No support

If **Federal** support, provide the sponsor information:

| Federal sponsor | Grant Title | Grant number | Awardee institution | Federal grant application |
|---|---|---|---|---|

For projects not supported by a federal grant, upload the research plan that was submitted for funding:

| Name | Modified Date |
|---|---|

If **Industry** support, provide the sponsor information and level of support:

If **Foundation** support, provide the sponsor information:

If **Other** support, provide the support information and level of support:

[reviewer notes¬]

**7.3** **Is this study funded in part or whole by a PHS Agency?**

* No

**Does any investigator* involved in this study (select all that apply):**

| | Name |
|---|---|
| [ ][ ] | **A.** Have a financial interest (aggregated value of equity and remuneration** during the past or next twelve months) in a **publicly-traded entity** that either sponsors*** this research or owns the technology being evaluated or developed that exceeds **$5,000 but not $10,000**? |
| [ ][ ] | **B.** Have a financial interest (aggregated value of equity and remuneration during the past or next twelve months) in a **publicly-traded entity** that either sponsors this research or owns the technology being evaluated or developed that exceeds **$10,000**? |
| [ ][ ] | **C.** Receive remuneration (during the past or next twelve months) from a **non-publicly traded entity** that either sponsors this research or owns the technology being evaluated or developed that exceeds **$5,000 but not $10,000**? |
| [ ][ ] | **D.** Receive remuneration (during the past or next twelve months) from a **non-publicly traded entity** that either sponsors this research or owns the technology being evaluated or developed that exceeds **$10,000**? |
| [ ][ ] | **E.** Have equity in a **non-publicly traded entity** that either sponsors this research or owns the technology being evaluated or developed? |
| [ ][ ] | **F.** Receive reimbursement or sponsorship of travel expenses (for one trip or a series of trips during the past or next twelve months) by an outside entity that either sponsors this research or owns the technology being evaluated or developed that exceeds **$5,000**? |

| | |
|---|---|
| [ ][ ] | **G.** Have rights as either the author or inventor of **intellectual property** being evaluated or developed in this research that is the subject of an issued patent or has been optioned or licensed to an entity? |
| [ ][ ] | **H.** Have an officer or management position**** with a **Licensed Start-up Company** overseen by the COI Committee that either sponsors this research or owns the technology being evaluated or developed? |
| [ ][ ] | **I.** Receive compensation of any amount when the value of the compensation would be affected by the outcome of this research, such as compensation that is explicitly greater for a favorable outcome than for an unfavorable outcome or compensation in the form of an equity interest in the entity that either sponsors this research or owns the technology being evaluated or developed? |
| [ ][ ] | **None** of the above options apply and there are no other financial conflicts of interest in the conduct of this research. |

***Investigator** means the PI, co-investigators, and any other member of the study team, regardless of title, who participates in the design, conduct, or reporting of this research, as well as his/her spouse, registered domestic partner, dependents, or other members of his/her household. **The PI is responsible for ensuring that s/he and all other relevant members of the study team review the above questions describing Significant Financial Interests.**

****such as salary, consulting fees, honoraria, or paid authorship

*****through the provision of funds, drugs, devices, or other support for this research

******Such as serving on the Board of Directors or Board of Managers or a position that carries a fiduciary responsibility to the company (e.g., CEO, CFO, CTO, or CMO).

## Does any investigator* involved in this study (select all that apply):

| | Name |
|---|---|
| [ ][ ] | **A.** Have equity in a **publicly-traded entity** that either sponsors** this research or owns the technology being evaluated or developed that exceeds a**5% ownership interest** or a current value of **$10,000**? |
| [ ][ ] | **B.** Have equity in a **non-publicly-traded entity** that either sponsors this research or owns the technology being evaluated or developed? |
| [ ][ ] | **C.** Receive salary, consulting fees, honoraria, royalties or other remuneration from an entity that either sponsors this research or owns the technology being evaluated or developed that is expected to exceed **$10,000** during the past or next 12 months? |
| [ ][ ] | **D.** Have rights as either the author or inventor of **intellectual property**being evaluated or developed in this research that is the subject of an issued patent or has been optioned or licensed to an entity? |

| | |
|---|---|
| [ ][ ] | **E.** Have an officer or management position**** with a **Licensed Start-up Company** overseen by the COI Committee that either sponsors this research or owns the technology being evaluated or developed? |
| [ ][ ] | **F.** Receive compensation of any amount when the value of the compensation would be affected by the outcome of this research, such as compensation that is explicitly greater for a favorable outcome than for an unfavorable outcome or compensation in the form of an equity interest in the entity that either sponsors this research or owns the technology being evaluated or developed? |
| **[X][X]** | **None of the above options apply and there are no other financial conflicts of interest in the conduct of this research.** |

*__Investigator__ means the PI, co-investigators, and any other member of the study team, regardless of title, who participates in the design, conduct, or reporting of this research, as well as his/her spouse, registered domestic partner, dependents, or other members of his/her household. **The PI is responsible for ensuring that s/he and all other relevant members of the study team review the above questions describing Significant Financial Interests.**

**through the provision of funds, drugs, devices, or other support for this research

****Such as serving on the Board of Directors or Board of Managers or a position that carries a fiduciary responsibility to the company (e.g., CEO, CFO, CTO, or CMO).

**7.3.1** **Provide the name of the investigator(s) and describe the nature of the Significant Financial Interest(s):**

**7.3.2**

*

| Name | Modified Date |
|---|---|

| | Section: Supporting Documentation |
|---|---|

[reviewer notes¬]

# Supporting Documentation Section

## References and Other Attachments

Additional documents:

| Name | Modified Date | Version |
|---|---|---|

Approved 3/9/2012 12:56 PM 0.01

[reviewer notes¬]

***ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.***

"Applicable clinical trials" are required **by federal law** to be registered in ClinicalTrials.gov.

Applicable Clinical Trials (ACTs) are studies that meet the following criteria:

- The study is an interventional study AND
- The study intervention is a drug, biologic, medical device, radiation or genetic AND
- The Study is not Phase 0 or 1 AND
- The study has at least one site in the United States or is conducted under an investigational new drug application or investigational device exemption

## NIH Policy

Effective January 18, 2017, revised NIH Policy requires that all clinical trials funded in whole or in part by the NIH be registered and results information posted on ClinicalTrials.gov.

As defined by the NIH, a clinical trial is:

*A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.*

The NIH Policy extends beyond the Food and Drug Administration Amendment Act (FDAAA 801) requirements in that it requires registration and results reporting of:

- clinical trials of behavioral, surgical and other types of health and medical interventions
- phase 1 studies of drugs and biological products
- small feasibility studies of device products

Failure to submit all required registration and results information requested on ClinicalTrials.gov can jeopardize University grant funding, the future funding of the grantee and subject the University of Pittsburgh to future monetary penalties.

In addition, to promote transparency of the clinical trials process, the International Committee of Medical Journal Editors (ICMJE) has established a policy requiring the entry of clinical trials in a public registry, such as ClinicalTrials.gov, prior to subject enrollment as a condition of consideration for publication of the trial results.

* **Based on the above information, will this study be registered in ClinicalTrials.gov?**

## Who will serve as the Responsible Party?

## Why are you registering your study? (Check all that apply)

There are no items to display

If you are not yet registered and need to establish an account for the PI or other research staff that may need to access the record, please send an email to the University of Pittsburgh PRS administrator at ctgov@pitt.edu with the following information for each individual:

- Full name
- Telephone number
- Pitt or UPMC email address

If you have any questions or concerns, please email us at ctgov@pitt.edu.

To find out additional information about how to register your study go to: https://www.clinicaltrials.gov/ct2/manage-recs/how-register