



**Adult to Adult
Living Donor Liver
Transplantation
Cohort Study**

A2ALL Cohort Protocol Manual of Operations

Inclusion/Exclusion Criteria for the Cohort Study Protocol

Inclusion Criteria for the Cohort Study Protocol

Potential recipients with an evaluated donor must fulfill all of the following criteria:

- Potential recipient listed for single organ (liver) transplantation
- Patient is eligible for LDLT
- Age \geq 18 years old at the time of donor history and physical exam
- Potential donor evaluated with history and physical examination at the transplant center
- Informed consent obtained.

Inclusion Criteria for the Cohort HCV Protocol

Patients with hepatitis C must fulfill all of the following criteria:

- Chronic hepatitis C virus infection and cirrhosis (may have concurrent HCC)
- HCV RNA positive (by qualitative or quantitative assay by local laboratory) pre-transplantation (within 6 months of transplant if not on treatment or within 2 weeks if on treatment)
- If subject joins study after transplant; subjects who are receiving treatment for HCV will be excluded from protocol biopsies.
- • Have none of the following conditions:
 - o Retransplantation (any cause)
 - o Fulminant hepatic failure
 - o Recipient of anti-HCV positive organ
 - o Recipient of anti-HBc positive organ
- Informed consent obtained.

Inclusion Criteria for the Cohort HCC Protocol

Patients with HCC must fulfill all of the following criteria:

- Diagnosis of hepatocellular carcinoma
- May have concomitant hepatitis C
- Informed consent obtained.

Inclusion Criteria for Donor controls

Contemporaneous DDLT controls must fulfill all of the following criteria:

- Potential recipient listed for single organ (liver) transplantation
- Age \geq 18 years old at transplant
- Indication for transplant: non-fulminant liver disease
- Informed consent obtained.

Inclusion Criteria for Donors in the Cohort Study Protocol

Donor candidates and donor control candidates must fulfill all of the following criteria:

- Meet donor criteria of the transplant center
- Be evaluated with a history and physical examination at the transplant center
- • Donor controls must have good health, or mild to moderate medical conditions that preclude donation but are not expected to impact their long-term quality of life or alter their natural history of survival/disease development compared to the normal population. Examples of acceptable conditions include:
 - o 10 % steatosis on biopsy with normal liver tests
 - o hemangioma/minor hepatic cystic disease on imaging precluding donor surgery
 - o diminutive liver or diminutive left lobe
 - o hepatic arterial or venous anatomical variations
 - o mild pulmonary hypertension
 - o hypercholesterolemia controlled with medication
 - o pregnancy
 - o recipient became non-LDLT candidate after donor approved.

Exclusion criteria for donor candidates in the Cohort study Protocol

Examples of unacceptable conditions include:

- o diabetes
- o hypertension
- o chronic hepatitis B or C
- o hypercholesterolemia not controlled on medication
- o diagnosis of cancer, excluding squamous cell and basal cell carcinoma of the skin
- o active substance abuse
- o major EKG abnormality or structural cardiac abnormality
- o moderate or severe pulmonary hypertension
- o psychiatric diagnosis



Definition of Adverse Event / Serious Adverse Event

Adverse event (AE)

An adverse event (AE) is any unfavorable, harmful or pathological change in a research subject as indicated by symptoms, physical signs and/or clinically significant laboratory abnormalities that occur in association with a study procedure(s) and may or may not be related to the study procedure(s). This definition includes intercurrent illness, injuries, exacerbation of pre-existing conditions, and events occurring as a result of the study procedure(s). Stable pre-existing conditions and elective procedures to address such conditions are not adverse events. A change in a laboratory variable is considered an adverse event if it was considered by the investigators to be clinically significant, or if it caused (or should have caused) the investigator to institute a diagnostic evaluation or additional therapy.

The term **serious** is based on patient outcome associated with events that could threaten a patient's life or functioning. An event should be considered serious if it results in any of the following:

- Death
- Life Threatening
- Inpatient/prolonged hospitalization
- Congenital anomaly or birth defect
- Persistent/significant disability or incapacity
- Medically important condition

The term **unexpected** means unobserved and undocumented. The following documents or circumstances will be used to determine the expectedness of an adverse event:

- Natural history of the disease under study
- Reports, which add significant information on specificity or severity of an otherwise known and documented adverse event, associated with the study procedure(s).

Liver transplantation is a complex procedure that may be associated with frequent and varied complications such as acute rejection, infections, metabolic disturbances, side effects of immunosuppressive medications and direct complications of surgery. Because this study involves patients who are candidates for liver transplant, who have a high frequency of infections, graft complications and renal insufficiency, events that meet the criteria of serious but are direct complications of liver diseases, and transplant surgery or expected side effects of anti-rejection medications will not be considered as AEs. (For recipients)

Liver donation is a complex procedure that may be associated with frequent and varied complications such as infections, transient impairment of liver function and direct complications of surgery. (For donors)

The following will be considered as adverse events resulting from the study protocol venipunctures:

- Bleeding
- Bruising
- Infection at the site
- Syncope

The following will be considered as adverse events resulting from the study protocol biopsies:

- Bleeding (occasionally severe)
- Bruising
- Infection at the site
- Pneumothorax
- Death

What should be recorded?

- Description and ICD-9 code for the event
- Date of onset
- Date of resolution
- Nature of the AE
- Severity
- Action taken – tests to evaluate AE, medications/procedures to treat AE

Each site is responsible for reporting all AEs and SAEs to the DCC. The DCC will be responsible for reviewing all AEs and SAEs. The DCC has the responsibility of reporting those events that are serious, unexpected and related to study procedures to the other sites. Each site is responsible for reporting serious unexpected study-related events that have occurred at other A2ALL clinical sites to their own IRB's at the time of study renewal.

The DCC will be responsible for notifying the DSMB of all AEs and SAEs at previously specified times during the course of the study. The DSMB will be notified in the form of reports and tables as previously determined.

Each site is responsible for submitting the DSMB reports to the IRB as progress reports for the study.

All deaths regardless of relatedness should be reported to the IRB within 7 days of notice.

All AEs that are serious, unexpected and related to study procedures need to be reported to all IRBs within 7 working days of receipt of reports.

All AEs that are serious, unrelated, and expected should be reported to the IRB at the renewal interval.

Data and Safety Monitoring Plan

Accepted principles of data and safety monitoring will be observed throughout the conduct of the A2ALL cohort study. Adverse Event and Serious Adverse Event reporting will follow the guidelines defined by this study. Since the study is largely observational the only research procedures that have the potential to generate an adverse event are venipuncture, liver biopsy, MRI and CT scans that exceed the standard of care at each institution.

Each transplant center principal investigator will be responsible for monitoring the A2ALL cohort study, as will the DCC. Monitoring responsibility will extend to determination of accurate and effective conduct of the protocol and to recommendations regarding closure of the study. The NIDDK has appointed an independent Data and Safety Monitoring Board (DSMB) that has approved the Cohort Study protocol and will continue to monitor the study's safety and progress.

Oversight of monitoring will be performed to ensure that: 1) monitoring activities are appropriate to the study, 2) monitoring is accomplished in a regular, timely and effective way and 3) recommendations that result from study monitoring are completed.

The Institutional Review Board (IRB) at each institution will approve the study and all subsequent amendments and modifications. The IRB will also be provided information on adverse events and study progress on a regular basis.

Training of study coordinators and study monitoring activities will be conducted by the DCC to ensure patient confidentiality and privacy, understanding of the study protocol and procedures and to maximize the reliability, accuracy, and timeliness of study data.

Data Management

All study data will be entered into the BioDBx electronic data entry system by study coordinators at each study site or entered by study subjects into the Keris tablet PC or online data capture page. This data will be encrypted and transferred to the DCC and will be stored on a secure server at the University of Michigan. Access to the server and BioDBx system is limited and requires a unique username and password combination. The servers are backed up daily and physically stored in a locked facility.

All analysis of the data sets will utilize de-identified (coded) data sets.

Quality Control and Database Management

The first steps in ensuring protocol compliance are good protocol design and careful orientation of study personnel. Following final agreement on protocols, and prior to study initiation at any of the transplant centers, the DCC will organize a Training and Certification session for transplant center study coordinators/data entry personnel.

The BioDBx electronic data entry system will have built-in data checks as part of study quality assurance. Protocol compliance will be assessed by monitoring the submission of

data at required intervals. Data inconsistencies and discrepancy reports will be reviewed by the Clinical Monitor so that necessary queries can be generated and sent to the transplant center study sites for verification and resolution.

Periodic requests may be generated for the submission of random source documents to assess the quality of data acquisition and data entry at each site. In addition, the Clinical Monitor or Project Manager will visit each site at least once to review source documents, monitor regulatory compliance, and assess protocol adherence.

In addition to source document verification, the Clinical Monitor and Project Manager will produce reports from the BioDBx system to look for inconsistencies in submitted data, particularly for repeated measures data elements, even if data do not fall outside of built-in validation routines.

Studies of intra-subject and inter-subject data variability by transplant center as well as intra-transplant center and inter-transplant center data variability will be used to further ascertain random or systematic data quality issues.

Comparisons of major endpoints from the current study to national data from the SRTR will be used to assess the extent to which participants in the A2ALL study are representative of the general population of patients undergoing these procedures in the United States.

Data Security/Data Transfer

Personnel at each study center will collect and enter data into BioDBx, a web-based data entry system. Authentication is currently enabled from Oracle Developer Form Server to the Oracle database. Between the web server and client browser, secure socket layer technology is in place. This will ensure safety and confidentiality of data by using secure encrypted data transmission from the transplant centers to the BioDBx database server.

The database logs every modification of every cell in the database to ensure the ability to monitor access to the data and audit transactions. The system is accessible only via an established account with a logon and password for security and confidentiality.

Authorized study personnel will be assigned an account on the system. Passwords will have defined expiration dates and must be changed regularly to permit continuing access.

The BioDBx database server is located in a locked cabinet in a locked room at the University of Michigan Medical Center. The hardware administrator and his designated backup are the only individuals who have keys. The data will be transferred via the secure network to the Kidney Epidemiology Cost Center (KECC) at the University of Michigan. The A2ALL project staff is physically located in the KECC office suite. The office suite is kept locked with entry control 24 hours a day to prohibit unauthorized entry.

The computer system at KECC currently is used for research projects that involve processing large volumes of identified and re-identifiable patient-specific data. The

KECC system has a comprehensive security plan based on the guidelines in OMB Circular A-130, "Security of Federal Automated Information Resources" and NIST Publication 800-18 "Guide for Developing Security Plans for Information Technology Systems." This plan has undergone extensive review by HRSA for security certification for maintaining patient-identified data. The A2ALL project will be covered by this security plan and will be required to comply.

A2ALL Cohort Protocol **Required Essential Documents**

Protocol Versions with Protocol Signature Sheets

All protocol versions must be included in the binder as well as the protocol signature sheets as they apply.

CV: Investigators and co-investigators

Must include current appointments/positions/citations, etc.

Must include start and end dates (or “to present”) for all appointments and positions (No date gaps).

CV should be signed and dated by the investigator (co-investigator) to verify document is current.

CV’s should be updated every two years.

CV SHOULD INCLUDE MEDICAL LICENSE NUMBER AND EXPIRATION DATE.

Medical License

A copy of current medical license with expiration date must be submitted for the PI and all co-investigators IF NOT included with the CV.

IRB/ERC Approvals

IRB/ERC approval letter MUST specifically state approval of the **PROTOCOL AND INFORMED CONSENT, AND/OR INVESTIGATORS BROCHURE**

Must be on IRB/ERC letterhead.

Actual date of IRB/ERC approval must appear on letter.

Protocol number, title and Version must appear on letter.

Renewal date or statement indicating when the approval must be renewed MUST be included in the letter.

Signature of the IRB/ERC Chairperson or designee must appear on the letter.

IRB Stamped Copy of Informed Consent

A copy of the approved consent is required

The copy must contain an IRB stamp of approval

IRB Membership List

Must be current.

If your IRB/ERC does not release its member ship list, a DHHS Multiple Assurance Number must be submitted on the IRB/ERC letterhead.

If any investigator or co-investigator is a member of the IRB/ERC, a letter or IRB/ERC meeting minutes indicating that the person abstained from voting on the protocol MUST be submitted.

Local Laboratory Information

Copy of the current Cap and CLIA Certification

Copy of current laboratory normal values for ALL protocol mandating testing (dates for which the normal values are applicable must be noted)

Hazardous Materials Certification

The individual responsible for packaging and shipment of serum/blood samples is required to have HazMat certification.

Human Research Subject Participation Certification

Certificate of Confidentiality

Subject Screening Log

Monitor Log

Major Correspondence (SAE Reports, DSMB Reports, Protocol Amendments)

Monitor Name: _____

Monitor Signature: _____ **Date:** _____

Additional Comments:

Laboratory Normals for the A2ALL Cohort Protocol

Please supply the DCC and maintain a copy in your regulatory binder a list of the following laboratory normals.

ALT

AST

Alk Phosphatase

Total bilirubin

Creatinine

Blood Urea Nitrogen (BUN)

Albumin

PT/PTT

INR

WBC

Ferritin

Hemoglobin

Platelets

Homocysteine

AFP

HCV RNA

Source Documentation / Regulatory Documents

Individual patient study binder

In addition to data entered into the BioDBx Program, all sites must keep a study binder for each patient enrolled. The study binder should include the following elements.

1. **Laboratory and Diagnostic Test Results**
 - a. **Inside Records** – Results of laboratory tests performed within the institution in which the patient has been enrolled can be kept in the existing reporting system. A copy of test results required for the study visits or evaluation of adverse events/recurrent HCV/recurrent HCC should be copied and placed in the study binder for monitoring purposes.
 - b. **Outside Records** – Results of any laboratory or diagnostic tests performed outside the institution in which the patient has been enrolled that are used for study visits, or evaluation of adverse events/recurrent HCV/recurrent HCC must be kept within the study binder and another copy in the medical record.
 - c. **Liver biopsy reports** – a copy of all liver biopsies performed pre and post-TXP should be included in the study binder.
 - d. **Radiology reports** – a copy of all radiologic imaging documenting diagnosis of HCC pre or post TXP or recurrent HCC post TXP should be included in the study binder.
2. **Clinic Notes / Source Documents for each study visit** - The dictated note from a clinic visit or procedure can be used as the source document for a particular visit. A copy of the note should be kept in the subject study binder with the corresponding visit.
3. **Consent Documents** – a signed and dated copy of the subjects' informed consent must be kept in the subjects' study binder. Be sure an original or copy of the original is placed within the subjects' hospital chart.
4. **Serious Adverse Event Reports** – Any reports submitted for subject SAEs should be kept in the subject study binder. The IRB must be informed of all SAEs. The report sent to the IRB for SAEs should be kept within the site Regulatory Binder. The IRB approval for continuation once the SAE has been reviewed should also be kept in the site Regulatory Binder.

MODEL CONSENT FORM - DONOR

INFORMATION ABOUT THIS DOCUMENT

You may be eligible to take part in a research study – to be a *subject* in an experiment or to let us use information about you to help us learn more about *living donor liver transplantation*. A primary objective of this study is to learn the long-term effects of donating the right lobe of the liver on the donor. This document gives you important information about the study. For example, it describes the purpose, risks, and possible benefits of participating in the study. Please take time to review this document carefully. After you have finished, you should discuss the information here, as well as any questions you have, with the researchers *and your doctor*. If you decide to take part in the study, you will be asked to sign this document. *Do not sign this form unless you understand what the study is about and the risks and possible benefits of participating.*

TITLE

A. Who is conducting this study?

_____ (Physicians names) are conducting a research study that is sponsored by the National Institutes of Health (NIH). Please take time to make your decision and discuss it with your friends and family. Remember that your participation is completely voluntary.

B. Why am I invited to participate in this study?

There are several reasons why you may be asked to be a part of this research study.

1. You are being asked to take part in this research study because *you are being evaluated as a donor for living donor liver transplantation. If you are accepted as a donor and undergo donor surgery your doctors plan to study the effect of the surgery on your liver and how the surgery impacts your health and quality of life. Even if you are not accepted as a donor and do not undergo the donor surgery, your doctors are interested in studying your progress.*
2. *You are being asked because you were already evaluated as a donor for a living liver donor transplant prior to the start of this study, and you are waiting for that donation to occur.*
3. *You are being asked because you were already evaluated as a donor for a living liver donor transplant prior to the start of the study, and you didn't donate.*

C. What is the purpose of this study?

A primary objective of this study is looking at the effects on the donor of donating the right lobe of the liver. Living donor liver transplantation is a new procedure. The single most important aspect of this procedure is the impact on the donor. There are many important questions which need to be answered regarding the long-term effect of undergoing donor surgery. This study is designed to determine the impact of donor surgery on several specific parts of your health and life. To answer these questions the study will measure:

- How well you are educated about the donation process by asking you questions about your understanding of the donor surgery.
- Specific details about your surgery.
- Any complications that you might experience immediately after the surgery as well as many months or years later.
- How fast your liver grows back after surgery and whether it reaches the same size as before the donor surgery.
- How the surgery impacts the quality of your day-to-day life after the surgery.

Since we need to know how the donation affects you months and years after surgery, we will need to perform tests on you immediately after the surgery and months and years later.

D. Are there Potential Conflicts of Interest?

The investigator of this research does not have any financial interest in the sponsor of this study. The treatments or procedures described in this document are not part of your standard care. You can choose not to participate in the research and still receive standard treatment from your physician.

Because your physician has an interest in this research, you may have questions or concerns about how your decision regarding participation in this research may affect the medical care you receive from your physician. Please feel free to discuss any questions or concerns with your provider. If you wish, you may also request to speak to another provider who is not a member of the research team.

E. How many people will take part in the study?

Approximately 1,400 people will take part in this NIH sponsored multi-center study, with the participation of nine major liver transplant centers around the United States.

F. What will I be asked to do?

If you agree to participate in this study we will ask you to undergo testing before the surgery, immediately after the surgery and each year until 2009. Many of the tests and procedures you will undergo are part of the normal course of your care. We are also asking you to provide samples of blood, liver tissue, and DNA (genetic material), which will be sent to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Central Repositories (storage facility), a research resource supported by the National Institutes of Health (NIH). The

Repository collects, stores, and distributes biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples available for use in research and teaching for the study of liver disease, after the current study is completed. Sending samples to the Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases.

If you are joining this study after you had been evaluated for a living liver donor transplant, it is likely you may have already gone through many of the tests and procedures listed here, because you've already passed these time points in your donation experience. If that's the case, we would like to collect information about you from your existing medical records and ask you to join the study at this point in your care and allow us to perform tests and procedures that are appropriate to your current status (either pre or post-transplant) and into the future.

We will ask you to do the following before the surgery:

- Answer approximately 100 survey questions about any bodily aches and pains you have and about your mood, expectations and quality of life
- Answer questions about your understanding of the donation evaluation process.
- Provide blood cell samples for the NIDDK Biosample and Genetics Repositories
- *(insert any other pre-operative tests that are not standard of care at the time points listed in the protocol)*

We will ask you to allow the researchers to perform the following tests on the day of your surgery:

- Provide a sample of liver to the NIDDK Biosample Repository.
- Allow the researchers to collect information about your donation surgery
- Allow the researchers to collect information about any complications you develop after your donation.
- *(insert a list of all tests that are not standard of care listed in the protocol for Day 0 at your facility)*

We will ask you to do the following immediately after your surgery:

- Provide blood samples during the first and second weeks after your donation to the NIDDK Biosample Repository.
- *(insert a list of all tests that are not standard of care listed in the protocol during the donation hospitalization).*

We will ask you to do the following throughout the course of the study:

- Provide blood samples to the NIDDK Biosample Repository at months 1, 3, 6, and 12, and annually thereafter until 2009.
- Return to the transplant center for assessment at months 1, 3, 6, and 12, and annually thereafter until 2009 *(delete timepoints that are standard of care at your facility)*
- Answer questions about your quality of life after donation (this does not apply to anyone enrolled after being evaluated as a donor) 3 and 12 months following donation and then yearly until 2009.

- Answer questions about your understanding of the donation process, the donation surgery, and post-operative expectations (this does not apply to anyone enrolled after being evaluated as a donor) 3 and 12 months following donation and then yearly until 2009.
- Allow the researchers to collect information about any complications you develop after your donation at months 1, 3, 6, and 12, and annually thereafter until 2009.
- Undergo a liver MRI (Magnetic Resonance Imaging-a standard imaging study) 3 months after your transplant to see how well your new liver is growing (*if this is not standard of care at your facility*)

If you are evaluated for living liver donation, but do not donate (for any reason) we would like to continue to have you complete the questionnaires at 3 months, 12 months and yearly from the date of your evaluation. We will not be collecting any further blood samples from you or conducting any other medical tests if you do not donate.

G. How long will I be in the study?

If you agree to participate in this study you will be asked to undergo testing until 2009.

H. Voluntary Withdrawal from Study

Participating in the study is completely **voluntary**. You do not have to participate. You may withdraw from the study at any time. You will not be penalized and will not lose any non-research benefits to which you otherwise may be entitled if you refuse to participate in the study or if you leave the study early. No aspect of your treatment (except the experimental procedures described below) or non-research benefits depends on your enrollment or continued participation in this or any other study.

If you decide to withdraw from this study, you will be requested to return “X” months after enrollment/transplant/donation for a physical examination and blood work (or other requested procedures). In addition, we would like to contact you from time to time to ask you a few questions regarding your health. Dr. (Physician) will discuss appropriate future treatment and procedures for your continued care.

If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the A2ALL study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the A2ALL study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample will stay in the Repository indefinitely.

I. What are the possible risks of the study?

It is important for you to understand that there is a small chance that some research may yield results that may indirectly have a negative impact on insurability, employability, and/or family relationships of some individuals or groups of people.

Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits may be paid back to the researchers and the organizations doing this study. You will not be charged for any of the development costs nor will you receive any financial benefits.

(Add your institution's boiler plate risk language for every procedure that is performed that is not standard of care at all time points in your facility, i.e. blood draw, liver biopsy, MRI, etc.)

J. Are there benefits to taking part in the study?

We cannot promise that you personally will receive any benefits from being in this study. You will not receive any direct benefit or payment for participating, but your sample may benefit the future health of the community at large or some particular group. Because other researchers will not have access to your identity, neither you nor your physician will get the eventual results of studies that might be performed using your sample.

It is possible that data resulting from use of your sample may eventually be used in a research publication. In that event, your name or other identifying information will not be included, as this information will not be available to the researchers.

K. What other options are there?

If you choose not to participate in this study, you will receive the same medical care and treatment given to all of the other donors.

L. What about confidentiality of my personal information?

All efforts will be made to keep your personal identification confidential. However, it is impossible to guarantee absolute confidentiality. Data from this study will be entered into a computerized database through a secured website. Only authorized personnel with a password will be permitted to enter or view the study data. Except as required by law, your research records will not be released without your prior written consent. If you authorize the release of your records, personnel are required by law to maintain the confidentiality of these records.

Organizations that may review your research records include: The National Institutes of Health; Food and Drug Administration (FDA); the Institutional Review Board (IRB), Data Management and Safety Board (DSMB), and the sponsor's representatives (Data Coordinating Center). If the results of the research are published, your name will not be used.

The Repository (central blood sample storage facility) will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before the researchers in this study send samples to the Repository, each sample will be given a code number. Your name and all personal identifying information, such as address, social security number, and date of birth, will

be removed. Therefore, the Repository will not be able to give out your name, or other information that identifies you to the scientists who receive the samples. However, the Repository and scientists will have some data about you, such as age, sex, diagnosis, {fill in any other data types}, race, and outcomes of the initial study. To help us protect your privacy, The Data Coordinating Center (DCC) and the Repository have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Why would my health information be disclosed?

There are many reasons why your health information may be used or disclosed in the course of this study. For example, the researchers may need the information to verify that you are eligible to participate in the study, or to monitor the results, including side effects. Other university and government officials, safety monitors, and study sponsors may need the information to ensure that the study is conducted properly. Also, information may need to be disclosed to insurance companies or others responsible for your medical bills in order to secure payment.

What information will be disclosed?

If you agree to participate in this study and sign your name on the last page, you will be giving the University Institution (hospitals, health centers, clinics and health care providers) and other providers involved in your care permission to disclose your medical information (doctors' notes, lab results, x-rays, hospital charts, etc.) to the researchers. This includes information relating to: Human Immunodeficiency Virus ("HIV") infection or Acquired Immunodeficiency Syndrome ("AIDS"); treatment for or history of drug or alcohol abuse; and/or mental or behavioral health or psychiatric care.

However, your name and other information that would directly identify you will not be used in any publications or presentations resulting from this research study, unless you give us separate written permission.

How will the researchers protect my privacy?

IRB No.:
Expiration Date:
Revised

Your research information will be stored in a locked cabinet and will not be made a part of your regular medical record. However, if the researcher orders any tests, the order and results may become part of your regular medical record. Study data submitted to the DCC will be entered in a secure website that requires a unique name and password and the data will be coded to protect your identity. All samples sent to the repository will contain a coded number instead of your name. Any publications that result from this study will not include any identifying information.

Other than the research staff, who might see information about me collected during the study, or other related medical records?

- ✓ Institution faculty, staff and contractors responsible for oversight of the research.
- ✓ Government officials who oversee research (such as the federal Office for Human Research Protections and the Food and Drug Administration).
- ✓ Safety monitoring boards that oversee the safety of this study.
- ✓ Research sponsors or funding sources and their representatives.
- ✓ Data Coordinating Center Staff

When does my permission expire? What happens to information about me after the study is over?

Your permission expires at the end of the study. However, even after the study is complete or after you decide to withdraw from the study, information about you may be used or disclosed as follows:

- ✓ To preserve the integrity of the other information collected during the study.
- ✓ As part of a data set used for research, educational and other lawful activities that does not include your name, social security number, or other identifying information.
- ✓ To Institution faculty, staff and agents responsible for oversight of the research.
- ✓ As required by applicable federal or state law. For example, if you withdraw from the study at any time, a record of your withdrawal and the reasons you gave for withdrawing will be kept as part of the study record. In addition, government officials who are responsible for oversight and review of clinical trials may require certain disclosures.

It is important to understand that once your medical records have been disclosed as described above, they may no longer be protected directly by federal privacy regulations issued under the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”).

M. What are the costs of my participation in this study?

There is no cost to you or to your insurance company for any of the research procedures in this study. However, you and your insurance company will be responsible for all costs associated with standard medical care provided to you during your participation in this research. These

costs include: surgical expenses, routine clinic visits, procedures, and medications that are part of your standard pre/post donation care.

N. Will I be paid?

You will not receive any pay for participation in this study. *(INSERT if any site compensation e.g. parking, food etc.)*

You should not expect to be reimbursed for lost income due to time away from work.

O. What happens if I need emergency care?

All forms of medical diagnosis and treatment, whether routine or experimental, involve some risk of injury. In spite of all safety measures, you might develop medical complications from participating in this study. In the event of injury or illness resulting from this study, you should contact the *(insert physician's name and number)*, the *(Hospital Emergency Room)* at *(Phone #)* or any physician or emergency room. Emergency medical treatment is available, but will be provided at the usual charge. No funds have been set aside to pay you in the event of injury, however, the *(insert Principal Investigator name)* will provide care for research-related injuries at no charge.

P. What are my rights as a human research participant?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled and will not affect the medical care you receive at *(Hospital Name)*.

We will tell you about any new information that may affect your health, welfare, or willingness to continue participation in the study.

Q. Whom do I call if I have questions or problems?

I have been informed that any new information that may affect my willingness to participate in this study will be given to me as it becomes available. If I need to find out more about any aspect of the study, including my rights, I may contact _____ *(Principal Investigator)* or any other attending physician listed on the front page of this consent document. If I have any other questions or concerns about my rights as a research subject, I may contact the Principal Investigator, _____ at _____ *(telephone number)*.

If you have any questions or concerns about your rights as a participant in a research study you may also contact the Medical Institutional Review Board. *(Please include IRB contact information here)*.

R. Consent Provisions

Your signature on this form indicates that:

You have had the opportunity to obtain answers to your questions concerning the nature of the experimental study, alternative treatments, if any, and potential discomforts, hazards, side-effects and risks related to the research study. You understand that there is a possibility that complications other than those described in this consent form may occur. You realize that although every effort will be made to keep all side effects to a minimum, side effects can be unpredictable both in nature and severity.

You understand that by consenting to participate in the study, you are not waiving any of your legal rights.

You hereby consent to voluntarily take part in the experimental study described above. You understand that you will be fully informed of any changes, which are to be made in this research, before such changes are made, that may affect you as a subject. You further understand that you will be informed of any significant new findings, which develop during the course of this research, which may influence your willingness to continue to participate.

You understand that any information that is obtained in connection with this research and that can be identified with you personally will remain confidential to the extent provided by law. You hereby consent to the release of medical information relating to the experimental study to the National Institutes of Health and the clinical investigators in the study for research purposes. You further consent to the publication in the medical literature of the results of this experimental research, upon the condition that your identity is not disclosed in such medical literature.

One copy of this document will be kept together with the investigators' research records on the study. A second copy will be given to you to keep. A third copy will be placed in your _____ *(institution name)* medical record.

(The remainder of this page is left intentionally blank to demonstrate that a portion of the consent text, and the entire signature block, should fit as shown on the following page.)

**ACKNOWLEDGED AND AGREED:
SIGNATURE BY THE SUBJECT:**

Please sign below if you agree to take part in this study.

- *you have read the informed consent and/or had it explained to you*
- *you were given the opportunity to ask questions about the information, and*
- *You can agree to one or both of the following*

You voluntarily agree to take part in the study

You voluntarily agree to provide blood, tissue, cell and information about your donation experience (this information does not contain your name or other identifying information) to the NIDDK Biosample, Genetics, and Data Repositories

_____ Research Subject's Name <i>(Typed or printed)</i>	_____ Research Subject's Signature	_____ Date
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OR

_____ Research Subject's Legal Guardian/Representative <i>(Typed or printed)</i>	_____ Legal Guardian's Signature	_____ Date
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_____ Witness's Name and title <i>(Typed or printed)</i>	_____ Witness's Signature	_____ Date
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(A witness to the research subject's signature is required.)

Signature of person explaining and obtaining the consent:

_____ Name and Title <i>(Typed or printed)</i>	_____ Signature	_____ Date
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(NOTE: This consent form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the research subject. A copy should be placed in the research subject's medical record, if applicable.)

MODEL CONSENT FORM - RECIPIENT

INFORMATION ABOUT THIS DOCUMENT

You may be eligible to take part in a research study – to be a *subject* in an experiment or to let us use information about you to help us learn more about [living donor liver transplantation](#). The primary study objective is to analyze the effect of choosing living donation rather than the wait for a deceased donor. This document gives you important information about the study. For example, it describes the purpose, risks, and possible benefits of participating in the study. Please take time to review this document carefully. After you have finished, you should discuss the information here, as well as any questions you have, with the researchers *and your doctor*. If you decide to take part in the study, you will be asked to sign this document. *Do not sign this form unless you understand what the study is about and the risks and possible benefits of participating.*

TITLE

A. Who is conducting this study?

_____ (Physicians names) are conducting a research study that is sponsored by the National Institutes of Health (NIH). Please take time to make your decision and discuss it with your friends and family. Remember that your participation is completely voluntary.

B. Why am I invited to participate in this study?

There are several reasons why you may be asked to be a part of this research study.

1. You are being asked to take part in this research study because [you are being evaluated as a recipient for living donor liver transplantation](#). If you have a living donor liver transplant your doctors plan to study the effect of the surgery on your liver and how the surgery impacts your health and quality of life. Even if you do not have the living donor liver transplant, your doctors are still interested in following your health status.
2. You are being asked because you were already evaluated as a candidate for a living liver donor transplant prior to the start of this study, and you are waiting for that transplant to occur.

3. Prior to the start of this study, you were evaluated as a candidate for a living liver donor transplant, and you received a living donor liver or a deceased donor liver transplant.

C. What is the purpose of this study?

The primary purpose of the study is to analyze the effect of choosing living donation rather than waiting for a deceased donor (DD). Living donor liver transplantation is a new procedure and there are many important questions, which need to be answered about this surgery. This study is designed to measure the safety and success and determine the impact of surgery on several specific parts of your health and life. To answer these questions the study will measure:

- Complications you experience while waiting for your transplant
- Specific details about your surgery to determine their impact on your long-term outcome.
- Complications that you might experience immediately after the surgery as well as many months or years later.
- How fast your liver grows back after surgery and whether it reaches the same size as before the donor surgery.
- How the surgery impacts the quality of your day-to-day life after the surgery.

Since we need to know how the donation affects you months and years after surgery, we will need to perform tests on you immediately after the surgery and months and years later.

D. Are there Potential Conflicts of Interest?

The investigator of this research does not have any financial interest in the sponsor of this study. The treatments or procedures described in this document are not part of your standard care. You can choose not to participate in the research and still receive standard treatment from your physician.

Because your physician has an interest in this research, you may have questions or concerns about how your decision regarding participation in this research may affect the medical care you receive from your physician. Please feel free to discuss any questions or concerns with your provider. If you wish, you may also request to speak to another provider who is not a member of the research team.

E. How many people will take part in the study?

Approximately 1,070 people will take part in this NIH sponsored multi-center study, with the participation of nine major liver transplant centers around the United States.

F. What will I be asked to do?

If you agree to participate in this study we will ask you to undergo testing before the surgery, immediately after the surgery and each year until 2009. Many of the tests and procedures you will undergo are part of the normal course of your care. We are also asking you to provide samples of blood, liver tissue, and DNA (genetic material), which will be sent to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Central Repositories (storage

facility), a research resource supported by the National Institutes of Health (NIH). The Repository will store and distribute biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples available for use in research and teaching for the study of liver disease, after the current study is completed. Sending samples to the Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases. The samples do not contain any identifying information. They have a code placed on the label to protect your privacy.

If you are joining this study after you had been evaluated for a living liver donor transplant, it is likely you may have already gone through many of the tests and procedures listed here, because you've already passed these time points in your transplant experience. If that's the case, we would like to collect information about you from your medical records and ask you to join the study at this point in your care and allow us to perform tests and procedures that are appropriate to your current status (either pre or post-transplant) and into the future.

We will ask you to do the following before the surgery:

- Answer approximately 75 survey questions about any bodily aches and pains you have and about your mood and quality of life
- Provide blood samples for the NIDDK Biosample and Genetics Repositories
- *(insert any other pre-operative tests that are not standard of care at the time points listed in the protocol)*
- If you are infected with Hepatitis C, we will ask you to do the following in addition to what is listed above before your liver transplant:
 - *(list pre-operative tests and procedures that are not standard of care for HCV patients at your facility)*
- If you have liver cancer (hepatocellular carcinoma-HCC), we will ask you to do the following in addition to what is listed above before your liver transplant:
 - *(list pre-operative tests and procedures that are not standard of care for HCC patients at your facility)*

We will ask you to allow the researchers to perform the following tests on the day of your surgery:

- Provide a sample of your old liver and your new liver to the NIDDK Biosample Repository.
- Allow the researchers to collect information about your transplant surgery.
- Allow the researchers to collect information about any complications you develop after your transplant.
- *(insert a list of all tests that are not standard of care listed in the protocol for Day 0 at your facility)*

We will ask you to do the following immediately after your surgery:

- Provide blood samples during the first and second weeks after your transplant to the NIDDK Biosample Repository.
- Answer approximately 100 survey questions about any bodily aches and pains you have and about your mood and psychological state

- *(insert a list of all tests that are not standard of care listed in the protocol during the transplant hospitalization).*
- If you have hepatitis C, we will ask you to undergo the following tests and procedures in addition to those listed above:
 - *(insert a list of all tests that are not standard of care listed in the protocol for HCV patients during the transplant hospitalization)*
- If you have liver cancer, we will ask you to undergo the following tests and procedures in addition to those listed above:
 - *(insert a list of all tests that are not standard of care listed in the protocol for HCC patients during the transplant hospitalization).*

We will ask you to do the following throughout the course of the study:

- Provide blood samples to the NIDDK Biosample Repository at months 1, 3, 6, and 12, and annually thereafter until 2009.
- Answer approximately 75 survey questions about any bodily aches and pains you have and about your mood and quality of life at 3 months, 12 months and annually thereafter until 2009.
- Return to the transplant center for assessment at months 1, 3, 6, and 12, and annually thereafter until 2009 *(delete timepoints that are standard of care at your facility)*
- Allow the researchers to collect information about any complications you develop after your transplant at months 1, 3, 6, and 12, and annually thereafter until 2009.
- Undergo a liver MRI 3 months after your transplant to see how well your new liver is growing *(if this is not standard of care at your facility)*
- If you have hepatitis C, we will ask you to undergo the following tests and procedures in addition to those listed above:
 - *(insert a list of all tests that are not standard of care listed in the protocol for HCV patients during the transplant hospitalization)*
- Provide a piece of your liver tissue (obtained in the course of either a routine or protocol biopsy) to the NIDDK Biosample Repository (this does not apply to patients who join the study after you have been evaluated for a living donor and have been treated for HCV)
- If you have liver cancer, we will ask you to undergo the following tests and procedures in addition to those listed above:
 - *(insert a list of all tests that are not standard of care listed in the protocol for HCC patients during the transplant hospitalization).*

G. How long will I be in the study?

If you agree to participate in this study you will be asked to undergo testing until 2009.

H. Voluntary Withdrawal from Study

Participating in the study is completely **voluntary**. You do not have to participate. You may withdraw from the study at any time. You will not be penalized and will not lose any non-research benefits to which you otherwise may be entitled if you refuse to participate in the study or if you leave the study early. No aspect of your treatment (except the experimental procedures described below) or non-research benefits depends on your enrollment or continued participation in this or any other study.

If you decide to withdraw from this study, you will be requested to return “X” months after enrollment/transplant/donation for a physical examination and blood work (or other requested procedures). In addition, we would like to contact you from time to time to ask you a few questions regarding your health. Dr. (Physician) will discuss appropriate future treatment and procedures for your continued care.

If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the A2ALL study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the A2ALL study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample will stay in the Repository indefinitely.

I. What are the possible risks of the study?

It is important for you to understand that there is a small chance that some research may yield results that may indirectly have a negative impact on insurability, employability, and/or family relationships of some individuals or groups of people.

Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits may be paid back to the researchers and the organizations doing this study. You will not be charged for any of the development costs nor will you receive any financial benefits.

(Add your institution’s boiler plate risk language for every procedure that is performed that is not standard of care at all time points in your facility, i.e. blood draw, liver biopsy, MRI, etc.)

J. Are there benefits to taking part in the study?

We cannot promise that you personally will receive any benefits from being in this study. You will not receive any direct benefit or payment for participating, but your sample may benefit the future health of the community at large or some particular group. Because other researchers will not have access to your identity, neither you nor your physician will get the eventual results of studies that might be performed using your samples.

It is possible that data resulting from use of your sample may eventually be used in a research publication. In that event, your name or other identifying information will not be included, as this information will not be available to the researchers.

K. What other options are there?

If you choose not to participate in this study, you will receive the standard medical care given to liver failure patients.

L. What about confidentiality of my personal information?

All efforts will be made to keep your personal identification confidential. However, it is impossible to guarantee absolute confidentiality. Data from this study will be entered into a computerized database through a secured website. Only authorized personnel with a password will be permitted to enter or view data. Except as required by law, your research records will not be released without your prior written consent. If you authorize the release of your records, personnel are required by law to maintain the confidentiality of these records.

Organizations that may review your research records include: The National Institutes of Health; Food and Drug Administration (FDA); the Institutional Review Board (IRB), Data Management and Safety Board (DSMB), and the sponsor's representatives (Data Coordinating Center). If the results of the research are published, your name will not be used.

The Repository (central blood sample storage facility) will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before the researchers in this study send samples to the Repository, each sample will be given a code number. Your name and all personal identifying information, such as address, social security number, and date of birth, will be removed. Therefore, the Repository will not be able to give out your name, or other information that identifies you to the scientists who receive the samples. However, the Repository and scientists will have some data about you, such as age, sex, diagnosis, {fill in any other data types}, race, and outcomes of the initial study. To help us protect your privacy, The Data Coordinating Center (DCC) and the Repository have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this

research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Why would my health information be disclosed?

There are many reasons why your health information may be used or disclosed in the course of this study. For example, the researchers may need the information to verify that you are eligible to participate in the study, or to monitor the results, including side effects. Other university and government officials, safety monitors, and study sponsors may need the information to ensure that the study is conducted properly. Also, information may need to be disclosed to insurance companies or others responsible for your medical bills in order to secure payment.

What information will be disclosed?

If you agree to participate in this study and sign your name on the last page, you will be giving the University/Institution (hospitals, health centers, clinics and health care providers) and other providers involved in your care permission to disclose your medical information (doctors' notes, lab results, x-rays, hospital charts, etc.) to the researchers. This includes information relating to: Human Immunodeficiency Virus ("HIV") infection or Acquired Immunodeficiency Syndrome ("AIDS"); treatment for or history of drug or alcohol abuse; and/or mental or behavioral health or psychiatric care.

However, your name and other information that would directly identify you will not be used in any publications or presentations resulting from this research study, unless you give us separate written permission.

How will the researchers protect my privacy?

Your research information will be stored in a locked cabinet and will not be made a part of your regular medical record. However, if the researcher orders any tests, the order and results may become part of your regular medical record. Study data submitted to the DCC will be entered in a secure website that requires a unique name and password and the data will be coded to protect your identity. All samples sent to the repository will contain a coded number instead of your name. Any publications that result from this study will not include any identifying information.

Other than the research staff, who might see information about me collected during the study, or other related medical records?

- ✓ Institution faculty, staff and contractors responsible for oversight of the research.
- ✓ Government officials who oversee research (such as the federal Office for Human Research Protections and the Food and Drug Administration).
- ✓ Safety monitoring boards that oversee the safety of this study.

- ✓ Research sponsors or funding sources and their representatives.
- ✓ Data Coordinating Center Staff

When does my permission expire? What happens to information about me after the study is over?

Your permission expires at the end of the study. However, even after the study is complete or after you decide to withdraw from the study, information about you may be used or disclosed as follows:

- ✓ To preserve the integrity of the other information collected during the study.
- ✓ As part of a data set used for research, educational and other lawful activities that does not include your name, social security number, or other identifying information.
- ✓ To Institution faculty, staff and agents responsible for oversight of the research.
- ✓ As required by applicable federal or state law. For example, if you withdraw from the study at any time, a record of your withdrawal and the reasons you gave for withdrawing will be kept as part of the study record. In addition, government officials who are responsible for oversight and review of clinical trials may require certain disclosures.

It is important to understand that once your medical records have been disclosed as described above, they may no longer be protected directly by federal privacy regulations issued under the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”).

M. What are the costs of my participation in this study?

There is no cost to you or to your insurance company for any of the research procedures in this study. However, you and your insurance company will be responsible for all costs associated with standard medical care provided to you during your participation in this research. These costs include: surgical expenses, routine clinic visits, procedures, and medications that are part of your standard pre/post transplant care.

N. Will I be paid?

You will not receive any pay for participation in this study. (*INSERT if any site compensation e.g. parking, food etc.*)

You should not expect to be reimbursed for lost income due to time away from work.

O. What happens if I need emergency care?

All forms of medical diagnosis and treatment, whether routine or experimental, involve some risk of injury. In spite of all safety measures, you might develop medical complications from participating in this study. In the event of injury or illness resulting from this study, you should contact the (*insert physician’s name and number*), the (*Hospital Emergency Room*) at (*Phone #*)

or any physician or emergency room. Emergency medical treatment is available, but will be provided at the usual charge. No funds have been set aside to pay you in the event of injury, however, the (*insert Principal Investigator name*) will provide care for research-related injuries at no charge.

P. What are my rights as a human research participant?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled and will not affect the medical care you receive at (*Hospital Name*).

We will tell you about any new information that may affect your health, welfare, or willingness to continue participation in the study.

Q. Whom do I call if I have questions or problems?

I have been informed that any new information that may affect my willingness to participate in this study will be given to me as it becomes available. If I need to find out more about any aspect of the study, including my rights, I may contact _____ (*Principal Investigator*) or any other attending physician listed on the front page of this consent document. If I have any other questions or concerns about my rights as a research subject, I may contact the Principal Investigator, _____ at _____ (*telephone number*).

If you have any questions or concerns about your rights as a participant in a research study you may also contact the Medical Institutional Review Board. (*Please include IRB contact information here*).

R. Consent Provisions

Your signature on this form indicates that:

You have had the opportunity to obtain answers to your questions concerning the nature of the experimental study, alternative treatments, if any, and potential discomforts, hazards, side-effects and risks related to the research study. You understand that there is a possibility that complications other than those described in this consent form may occur. You realize that although every effort will be made to keep all side effects to a minimum, side effects can be unpredictable both in nature and severity.

You understand that by consenting to participate in the study, you are not waiving any of your legal rights.

You hereby consent to voluntarily take part in the experimental study described above. You understand that you will be fully informed of any changes, which are to be made in this research, before such changes are made, that may affect you as a subject. You further

understand that you will be informed of any significant new findings, which develop during the course of this research, which may influence your willingness to continue to participate.

You understand that any information that is obtained in connection with this research and that can be identified with you personally will remain confidential to the extent provided by law. You hereby consent to the release of medical information relating to the experimental study to the National Institutes of Health and the clinical investigators in the study for research purposes. You further consent to the publication in the medical literature of the results of this experimental research, upon the condition that your identity is not disclosed in such medical literature.

One copy of this document will be kept together with the investigators' research records on the study. A second copy will be given to you to keep. A third copy will be placed in your _____ *(institution name)* medical record.

(The remainder of this page is left intentionally blank to demonstrate that a portion of the consent text, and the entire signature block, should fit as shown on the following page.)

**ACKNOWLEDGED AND AGREED:
SIGNATURE BY THE SUBJECT:**

Please sign below if you agree to take part in this study.

- *you have read the informed consent and/or had it explained to you*
- *you were given the opportunity to ask questions about the information, and*
- *You can agree to one or both of the following*

You voluntarily agree to take part in the study

You voluntarily agree to provide blood, tissue, cell and information about your transplant experience (this information does not contain your name or other identifying information) to the NIDDK Biosample, Genetics, and Data Repositories

_____ Research Subject's Name <i>(Typed or printed)</i>	_____ Research Subject's Signature	_____ Date
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OR

_____ Research Subject's Legal Guardian/Representative <i>(Typed or printed)</i>	_____ Legal Guardian's Signature	_____ Date
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_____ Witness's Name and title <i>(Typed or printed)</i>	_____ Witness's Signature	_____ Date
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(A witness to the research subject's signature is required.)

Signature of person explaining and obtaining the consent:

_____ Name and Title <i>(Typed or printed)</i>	_____ Signature	_____ Date
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(NOTE: This consent form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the research subject. A copy should be placed in the research subject's medical record, if applicable.)



INFORMATION FOR PROSPECTIVE SUBJECTS – DONOR CANDIDATES

You may be eligible to take part in a research study that will use information about you to help us learn more about **living donor liver transplantation**. A primary objective of this study is to learn the long-term effects of donating the right lobe of the liver on the donor. We want to study how the surgery affects your health and quality of life. We're also interested in studying how long it takes your liver to grow back after you've donated a portion of it. Another goal is to identify what makes someone want to donate a portion of their liver to another person, and to study how well we explain the evaluation, surgery and recovery process.

The study is called the Adult to Adult Living Donor Liver Transplantation Cohort Study (A2ALL) and is being conducted by researchers at 9 leading transplant centers around the United States. The study is sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), with additional funding from the Health Resources and Services Administration (HRSA) and the American Society of Transplant Surgeons (ASTS).

The A2ALL project is an observational study that will be carried out until 2009. We want to observe and monitor the health and well-being of participants during the pre- and post-donation experience. Almost all of the tests are done as part of your normal course of care even if you weren't enrolled in the A2ALL study. However, if you choose to enroll in the study, you will be asked to give some additional blood and liver samples beyond what you would normally experience during the course of your clinical care at the transplant center. We'll also ask you to answer a series of questionnaires. Your name and other identifying information will not be used in the study.

There are no direct medical benefits to you for participating in this study. There are some risks associated with donating blood samples and liver tissue. If you are interested in participating in the study, these risks will be explained to you in detail.

If you want to participate in this study, you must give your permission by signing a consent form. Please contact the transplant center for more information. Note that participation is available only to patients who are cared for at one of the nine transplant center members of the A2ALL project. If you choose not to participate in this study, it won't change the care you receive at the transplant center.



INFORMATION FOR PROSPECTIVE SUBJECTS – RECIPIENT CANDIDATES

You may be eligible to take part in a research study that will use information about you to help us learn more about **living donor liver transplantation**. The primary study objective is to learn whether it's better to receive a liver transplant from a living donor or to wait for a deceased donor. The team doing the study wants to compare recipients who receive living donor transplants (LDLT) to those who do not, including patients who receive deceased donor transplants (DDLT). We want to study how the surgery affects your health and quality of life. We are also studying the effects of the donation evaluation process and liver donation surgery itself on living donors.

The study is called the Adult to Adult Living Donor Liver Transplantation Cohort Study (A2ALL) and is being conducted by researchers at 9 leading transplant centers around the United States. The study is sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), with additional funding from the Health Resources and Services Administration (HRSA) and the American Society of Transplant Surgeons (ASTS).

The A2ALL project is an observational study that will be carried out until 2009. We want to observe and monitor the health and well-being of participants during the pre- and post-transplant experience. Almost all of the tests are done anyway as part of your normal course of care even if you weren't enrolled in the A2ALL study. However, if you choose to enroll in the study, you will be asked to give some additional blood and liver samples beyond what you would normally experience. We will also ask you to respond to a series of questionnaires. Your name and other identifying information will not be used in the study.

There are no direct medical benefits to you for participating in this study. There are some risks associated with donating blood samples and liver tissue. If you are interested in participating in the study, these risks will be explained to you in detail.

If you want to participate in this study, you must give your permission by signing a consent form. Please contact the transplant center for more information. Note that participation is available only to patients who are cared for at one of the nine transplant center members of the A2ALL project. If you choose not to participate in this study, it won't change the care you receive at the transplant center.

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Recipients:

Time Point	Forms	Samples/Procedures	Comments
Enrollment	<ul style="list-style-type: none"> RCP Demographics RCP Condition @ Enrollment QOL Assessment (SF-36) HCC @ Enrollment HCV @ Enrollment 	<ul style="list-style-type: none"> 3 ACD tubes whole blood-Rutgers HLA Typing 15 ml of blood for serum, labs, AFP Imaging for HCC HCV labs 	<p>24 ml whole blood</p> <p>10 serum aliquots 0.4ml each</p>
Pre-TXP Quarterly Assessment 1-5	<ul style="list-style-type: none"> RCP Pre-TXP Quarterly Assessment 1-5 QOL Assessment (SF-36) HCC Pre-TXP Quarterly Assessment 1-5 HCV Pre-TXP Quarterly Assessment 1-5 RCP Hospitalizations 	<ul style="list-style-type: none"> 15 ml of blood for serum, labs, AFP Imaging for HCC Labs for HCV 	<p>10 serum aliquots 0.4ml each</p> <p>Each hospitalization requires a separate form.</p>
Transplant	<ul style="list-style-type: none"> RCP Condition @ TXP RCP Intraop HCC @ TXP HCC Explant Assessment HCV @ TXP RCP Hospitalizations AE/SAE Form 	<ul style="list-style-type: none"> 1 Tru-cut Bx-back table, cut into thirds; 2 in RNALater, 1 in formalin 1 Tru-cut Bx 30-60 minutes post-reperfusion cut into thirds; 2 in RNALater, 1 in formalin 15 ml blood for serum , labs, pre-op 15 ml blood for serum at the same time points of the Bx's (anhepatic & 30-60 minutes post-reperfusion) HepB and HCV status of donor for DDLT recipients HCV labs 	<p>The TXP counts as a hospitalization and may be completed at discharge visit</p> <p>Each blood draw = 10 serum aliquots 0.4ml each</p>
Day 1 post-txp	None	<ul style="list-style-type: none"> 15 ml blood for serum 	10 serum aliquots 0.4ml each

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Recipients:

Time Point	Forms	Samples/Procedures	Comments
Week 1 Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 1 Week Post-TXP RCP Morbidity RCP Hospitalizations Rejection Episodes AE/SAE Form HCV @ 1 Week Post-TXP 	<ul style="list-style-type: none"> 15 ml blood for serum, labs *1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin HCV labs 	<p>10 serum aliquots 0.4ml each</p> <p>*Bx only if rejection episode</p> <p>Each hospitalization, morbidity and rejection episode requires own form</p>
2 Weeks Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 2 Weeks Post-TXP RCP Morbidity RCP Hospitalizations Rejection Episodes AE/SAE Form 	<ul style="list-style-type: none"> 15 ml blood for serum, labs *1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin 	<p>10 serum aliquots 0.4ml each</p> <p>*Bx only if rejection episode</p> <p>Each hospitalization, morbidity and rejection episode requires own form</p>
1 Month post TXP	<ul style="list-style-type: none"> RCP Condition @ 1 Month Post-TXP HCV @ 1 Month Post-TXP HCV Biopsy Pathology Report RCP Morbidity RCP Hospitalizations Rejection Episodes AE/SAE Form 	<ul style="list-style-type: none"> 15 ml blood for serum, labs HCV labs *1 Tru-cut Bx prior to treatment of HCV recurrence; cut into thirds; 2 in RNALater, 1 in formalin **1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin 	<p>10 serum aliquots 0.4ml each</p> <p>*Bx only if treated HCV recurrence</p> <p>**Bx only if rej. episode</p> <p>Each hospitalization, morbidity and rejection episode requires own form</p>

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Recipients:

Time Point	Forms	Samples/Procedures	Comments
3 Months Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 3 Months Post-TXP QOL Assessment (SF-36) HCV @ 3 Months Post-TXP HCV Bx Pathology Report RCP Morbidity RCP Hospitalizations Rejection Episodes AE/SAE Form & Tracking Form 	<ul style="list-style-type: none"> 15 ml blood for serum, labs, AFP Protocol Bx for HCV patients: 1 Tru-cut Bx cut into thirds; 2 in RNALater, 1 in formalin *Bx: 1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin MRI/CT to measure liver volume for Regeneration study (day 91) Prednisone dose in mg. 	<p>10 serum aliquots 0.4ml each</p> <p>*Bx only if rejection episode or treated HCV recurrence</p> <p>Each hospitalization, morbidity and rejection episode requires its own form</p>
6 Months Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 6 Months Post-TXP QOL Assessment (SF-36) RCP Morbidity HCV Bx Pathology Report HCC @ 6 Months Post-TXP RCP Hospitalizations Rejection Episodes AE/SAE Form 	<ul style="list-style-type: none"> 15 ml blood for serum, labs, AFP HCC Imaging *Bx: 1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin **1 Tru-cut Bx prior to treatment of HCV recurrence; cut into thirds; 2 in RNALater, 1 in formalin 	<p>10 serum aliquots 0.4ml each</p> <p>*Bx only if rejection episode</p> <p>Each hospitalization, morbidity and rejection episode requires own form</p> <p>**Bx only if treated HCV recurrence</p>

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Recipients:

Time Point	Forms	Samples/Procedures	Comments
1 Year Post-TXP	<ul style="list-style-type: none"> • RCP Condition @ 1 Year Post-TXP • QOL Assessment (SF-36) • HCC @ 1 Year Post-TXP • HCV @ 1 Year Post-TXP • HCV Bx Pathology Report • RCP Morbidity • RCP Hospitalizations • Rejection Episodes • AE/SAE Form 	<ul style="list-style-type: none"> • 15 ml blood for serum, labs, AFP • Protocol Bx for HCV patients: 1 Tru-cut Bx cut into thirds; 2 in RNALater, 1 in formalin • HCC Imaging • HCV labs • *1 Tru-cut Bx prior to treatment of HCV recurrence; cut into thirds; 2 in RNALater, 1 in formalin • **1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin 	<p>10 serum aliquots 0.4ml each</p> <p>Each hospitalization, morbidity and rejection episode requires its own form</p> <p>*Bx only if treated HCV recurrence</p> <p>**Bx only if rejection episode</p>
18 Mos Post-TXP	<ul style="list-style-type: none"> • HCC @ 18 Months Post-TXP 	<ul style="list-style-type: none"> • AFP 	HCC patients only
2 Years Post-TXP	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP 	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP 	Same as 1 Yr Post-TXP
3 Years Post-TXP	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP 	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP except no HCC imaging 	Same as 1 Yr Post-TXP
4 Years Post-TXP	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP 	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP except no HCC imaging and no HCV Protocol Bx 	Same as 1 Yr Post-TXP
5 Years Post-TXP	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP 	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP except no HCC imaging and no HCV Protocol Bx 	Same as 1 Yr Post-TXP

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Donors:

Time Point	Forms	Samples	Comments
Enrollment/Donor Evaluation	<ul style="list-style-type: none"> • Donor Demographics • Donor Evaluation • Full QOL and Motivation 	<ul style="list-style-type: none"> • 3 ACD tubes of whole blood to Rutgers Genetics repository • 15 ml blood draw for serum, labs • Homocysteine level 	<p>24 ml whole blood</p> <p>10 serum aliquots 0.4ml each</p>
At Donation	<ul style="list-style-type: none"> • Donor Intraop • Donor Hospitalizations 	<ul style="list-style-type: none"> • HLA Typing • 1 Tru-cut Bx prior to removal, cut into thirds; 2 in RNALater, 1 in formalin • 15 ml blood for serum, labs pre-op • 15 ml blood for serum at the same time as the Bx • 15 ml blood for serum 30-60 min. after crossclamp 	<p>The donation surgery counts as a hospitalization and form may be completed at discharge visit</p> <p>Each blood draw = 10 serum aliquots 0.4ml each</p>
Day 1 post-txp	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • 15 ml blood for serum, labs 	
1 Week Post-Donation	<ul style="list-style-type: none"> • Donor Condition @ 1 Week Post-Donation • Donor Hospitalizations • Donor Morbidity/Complications • AE/SAE Form 	<ul style="list-style-type: none"> • 15 ml blood for serum, labs 	<p>10 serum aliquots 0.4ml each</p> <p>Each hospitalization and morbidity requires a separate form</p>
1 Month Post-Donation	<ul style="list-style-type: none"> • Donor Condition @ 1 Mon. Post-Donation • Donor Hospitalizations • Donor Morbidity/Complications • AE/SAE Form 	<ul style="list-style-type: none"> • 15 ml blood for serum, labs 	<p>10 serum aliquots 0.4ml each</p> <p>Each hospitalization and morbidity requires a separate form</p>

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Donors:

Time Point	Forms	Samples/Procedures	Comments
3 Months Post-Donation	<ul style="list-style-type: none"> • Donor Condition @ 3 Mos Post-Donation • Full QOL and Motivation • Donor Hospitalizations • Donor Morbidity/Complications • AE/SAE Form 	<ul style="list-style-type: none"> • 15 ml blood for serum, labs • MRI/CT for Regeneration study (day 91) 	<p>10 serum aliquots 0.4ml each</p> <p>Each hospitalization and morbidity requires a separate form</p>
1 Year Post-Donation	<ul style="list-style-type: none"> • Donor Condition @ 1 Year Post-Donation • Full QOL and Motivation • Donor Hospitalizations • Donor Morbidity/Complications • AE/SAE Form 	<ul style="list-style-type: none"> • 15 ml blood for serum, labs 	<p>10 serum aliquots 0.4ml each</p> <p>Each hospitalization and morbidity requires a separate form</p>
2 Yrs Post-Donation	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	Same as 1 Yr Post Donation
3 Yrs Post-Donation	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	Same as 1 Yr Post Donation
4 Yrs Post-Donation	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	Same as 1 Yr Post Donation
5 Yrs Post-Donation	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	Same as 1 Yr Post Donation

Cohort Protocol Recipient & Donor Schedule of Visits and Assessments (narrative)

Visit Schedule and Assessments:

After obtaining the subject's informed consent for participation in the study, the following assessments will be performed according to the visit schedule. Subjects recruited from the A2ALL Retrospective Study will join the cohort visit schedule from whatever clinical point they are at in their transplant or donation experience. Exceptions to this would be informed consent assessments for donors and protocol biopsies for subjects who are undergoing treatment for recurrent HCV post-transplant. Tables summarizing the visit schedules for donors and recipients with accompanying tests and procedures are included as Appendices A and B.

Since the study is primarily an observational investigation, it should be remembered that many of the assessments listed below are included in what is considered standard of clinical care in many institutions, and therefore would not require additional visits or sample collections from the patient.

Enrollment – Recipients:

- Medical history
- Social history
- Demographic information
- Physical examination: including weight, blood pressure, etc.
- Routine laboratory assessment: blood will be drawn to obtain values for the following tests: multichannel automated liver function tests, AFP, albumin, creatinine, and coagulation panels
- Blood sample will be drawn for HLA typing
- Blood sample for NIDDK Biosample Repository
- Cell sample for NIDDK Genetics Repository
- Quality of life baseline assessment
- HCV-infected subjects will undergo the following laboratory assessments in addition to those listed above:
 - HCV RNA quantitative or qualitative assay
 - HCV genotype (if not done previously)
- Subjects with HCC will also undergo the following imaging studies if not done within 3 months previous to study enrollment:
 - Bone scan
 - Chest CT
 - Abdominal MRI/contrast CT

Pre-transplant Interval Assessments – Recipients:

The following assessments will be performed quarterly from the time of enrollment until transplant (or subject death if it occurs prior to transplant):

- Physical examination: including weight, blood pressure, etc.
- Routine laboratory assessment: blood will be drawn to obtain values for the following tests: multichannel automated liver function tests, AFP, albumin, creatinine, and coagulation panels
- Quality of life interval assessment: quarterly and one week prior to transplant
- HCV-infected subjects will undergo the following laboratory assessments in addition to those listed above:
 - HCV RNA quantitative or qualitative assay
- Subjects with HCC will also undergo the following imaging studies
 - Bone scan
 - Chest CT
 - Abdominal MRI/contrast CT

Enrollment – Donors:

- Medical history
- Social history
- Demographic information
- Physical examination: including weight, blood pressure, etc.
- Routine laboratory assessment: blood will be drawn to obtain values for the following tests: multichannel automated liver function tests, albumin, creatinine, coagulation panels, white blood cell count, hemoglobin, ferritin, platelets, blood urea nitrogen (BUN), homocysteine
- Screening lab values: CMV IgG/IgM, HIV Antibody, Hepatitis B core antibody (HBcAb), Hepatitis B surface antigen (HBsAg), Hepatitis C Antibody, HCV RNA (if HepC positive), Hepatitis D Antibody (if HepB positive)
- Blood sample for NIDDK Biosample Repository
- Cell sample for NIDDK Genetics Repository
- Liver MRI
- Quality of life baseline assessment
- Informed consent baseline assessment (comprehension and understanding, motivation for decision-making, and satisfaction with treatment)

Day of Transplant – Recipients:

- Allograft biopsy and analysis
- Routine Laboratory Assessment: blood will be drawn to obtain values for the following tests: multichannel automated liver function tests, AFP, albumin, creatinine, and coagulation panels
- Explant pathology analysis
- Tissue sample for NIDDK Biosample Repository
- Blood sample for NIDDK Biosample Repository
- HCV-infected subjects will undergo the following laboratory assessments in addition to those listed above:
 - HCV RNA quantitative or qualitative assay

- Subjects with HCC will undergo the following laboratory assessments in addition to the routine laboratory assessments listed above:
 - Detailed pathological analysis of explant liver with tumor staging

Day of Donation – Donors:

- Allograft biopsy and analysis
- Routine laboratory assessment: blood will be drawn to obtain values for the following tests: multichannel automated liver function tests, albumin, creatinine, coagulation panels, white blood cell count, hemoglobin, ferritin, platelets, BUN
- Blood sample will be drawn for HLA typing
- Tissue sample for NIDDK Biosample Repository
- Blood sample for NIDDK Biosample Repository

Post-transplant Interval Assessments – All Recipients:

The following assessments and procedures will be performed post-operatively at Week 1 and 2, Months 1, 2, 3, 6 and 12, and annually thereafter until the study is complete or the subject reaches a study endpoint.

- Physical examination: including weight, blood pressure, etc.
- Routine laboratory assessment: blood will be drawn to obtain values for the following tests: multichannel automated liver function tests, albumin, AFP, creatinine, and coagulation panels
- Blood sample for NIDDK Biosample Repository
- Quality of life interval assessments at 3, 6, and 12 months and annually thereafter
- Liver MRI at Month 3 only.

Post-transplant Interval Assessments – HCV-infected Recipients:

In addition to the assessments listed above, HCV-infected recipients will undergo the following assessments at the following time points:

- Week 1, Month 1, Year 1, 2, and 3: HCV RNA quantitative or qualitative analysis
- Month 3, Year 1, 2 and 3: Liver biopsy
- Month 3, Year 1, 2 and 3: Tissue sample for NIDDK Biosample Repository

Post-transplant Interval Assessments – Subjects with HCC:

In addition to the assessments listed above for all recipients, recipients with HCC will undergo the following assessments at Months 6, 12, 18 and 24:

- Serum AFP (at month 18 in addition to AFP's done at interval assessments for all recipients)
- Abdominal MRI/contrast CT: at months 6, 12 and 24 only.

Subjects Showing Signs and Symptoms of Allograft Rejection:

Subjects showing signs and symptoms of allograft rejection will undergo a liver biopsy with analysis to confirm the diagnosis of rejection. A biopsy will be performed to confirm each rejection episode. A tissue sample from these biopsies will also be sent for storage at the NIDDK Biosample Repository.

Post-Donation Assessments – Donors:

The following assessments will be performed for donors at Week 1, and Months 1, 3, and 12, and annually thereafter until the study is complete or the donor reaches a study endpoint or is lost to follow-up:

- Routine laboratory assessment: blood will be drawn to obtain values for the following tests: multichannel automated liver function tests, albumin, creatinine, coagulation panels, white blood cell count, hemoglobin, ferritin, platelets, BUN
- Blood sample for NIDDK Biosample Repository
- Liver MRI at month 3 only
- Quality of life assessment: limited to a pain survey at Week 1 and Month 1. Donor and donor controls will undergo the full battery of QOL assessments at Months 3, 12 and annually thereafter.
- Informed consent assessment (satisfaction with treatment): at Months 1, 3, and 12, and annually thereafter
- Informed consent assessment (motivation): at Week 1, Months 3 and 12, and annually thereafter.



Adding A Subject

1. Sign on to BioDBx
2. Click on the “Enroll New Subject Button”
3. Fill in the information requested. Be careful, because once you save this information you will not be able to edit it.
4. Assign the subject class that’s appropriate to your subject from the drop-down box. The choices are:
 - Donor Control (DC)
 - Donor (D)
 - Recipient Candidate (R)
 - Recipient Candidate with HCV (V)
 - Recipient Candidate with HCC (C)
 - Recipient Candidate with HCC and HCV (CV)
5. If a subject’s class changes during the course of the study, you will have to request that the DCC assign a new subject class to that individual.
6. Save the information. The system will automatically assign a subject ID.

Enroll New Subject

Show All Subjects

Search for Subject

Current User: Joe Bonner [Log

Current Study: A2COH

Current Site: Test

Demo Web Pages

Study Subject: Update

Age: _____

PX_ID: _____

Gender: Female Male

Subject: R1017 _____

Race: _____

Date of Consent: _____

Removed from Study? _____

Class: Recipient _____

Save Clear



Matching Recipients & Donors in Cohort Study

1. Completely fill out the PHI page on both the Donor and the Recipient. Make sure you note the Donor's BioDBx ID number, Date of Birth, Gender and Ethnicity.
2. Open up the Recipient's PHI page.
3. Scroll down to the Subject Relationships Table.
 - Note that if the subject is also enrolled in the LADR study, there may be an "also known as (AKA)" relationship established denoting the subject's LADR enrollment.

Current Subject: R1735

- Enter Data
- Enrollment 08-26-2005
- Qtr1
- Qtr2
- Qtr3
- Qtr4
- Qtr5
- Txp/Dntn Surg
- vWeek 1
- vWeek 2
- Month 1
- Month 3
- Month 6
- Month 12
- Month 18
- Month 24
- Month 36
- Month 48
- Month 60
- Rejection
- Hospitalization
- Complication/Morbidity Event
- Year 6 (Month 72)
- Year 7 (Month 84)
- Year 8 (Month 96)

Date of Birth: 10/12/1967

Gender: Male

Subject: R1735

Race: Hispanic - Black or African American

Date of Consent: 08/26/2005

Removed from Study?

Class: Recipient

Comment:

[Save](#) [Clear](#)

Subject Relationships

[Add a Relationship](#)

AKA [A2LADR-R1735](#)

- Click on the “Add a Relationship” link. A new window will open up in your browser. Scroll down until you see the donor ID, birth date, gender and ethnicity of the donor that you are linking to this recipient.

Add relationship for subject R1735 in A2COH study T site

Relationship Type

Select a Donor:

- D1822,14-MAR-60,Female,White/Caucasian
- D1810,25-MAR-77,Female,AmericanIndian/AlaskanNative
- D1764,30-JUN-59,Male,Asian
- D1395,06-JUL-79,Female,Black/African American
- D1394,06-FEB-69,Male,Hispanic - American Indian or Alaska Native
- D1313,05-NOV-57,Female,Black/African American
- D1066,03-NOV-66,Male,AmericanIndian/AlaskanNative
- D1049,30-JUN-61,Female,Hispanic - White
- D1033,14-FEB-59,Male,White/Caucasian
- D1027,25-DEC-80,Male,White/Caucasian
- D1016,05-NOV-57,Female,NativeHawaiian/PacificIslander
- D1010,08-SEP-79,Male,White/Caucasian
- D1009,21-JAN-73,Female,NativeHawaiian/PacificIslander**
- D1008,19-NOV-83,Male,Hispanic - American Indian or Alaska Native
- D1007,31-OCT-75,Female,Black/African American
- D1006,21-APR-84,Male,Hispanic - White
- D1005,06-JUL-79,Female,White/Caucasian
- D1004,15-AUG-56,Male,White/Caucasian
- D1003,12-OCT-53,Female,Black/African American
- D1002,07-JUN-75,Male,Hispanic - American Indian or Alaska Native

- Click the “Create Relationship” button.

Add relationship for subject R1735 in A2COH study T site

Relationship Type

Select a Donor:

- A “success” message will tell you that you have successfully linked the two subjects.

Relation is created successfully!

Close

- Click the “Close” button. The window will close and you’ll be back at the Recipient’s PHI page. Right click on the frame and select “Refresh”. The newly created relationship will appear in the Subject Relationships table.

Subject: R1735

Race: Hispanic - Black or African American

Date of Consent: 08/26/2005

Removed from Study?

Class: Recipient

Comment:

Subject Relationships

[Add a Relationship](#)

AKA A2LADR-R1735	
Matched With A2COH-D1009	Remove Relationship

- If you click on the Donor ID number in the Recipient’s Subject Relationships table, it will bring up the Donor’s PHI page for confirmation.

https://cric.cacr.med.umich.edu/pls/biodbx01/A2COH_STUDY.cds.build_subject_template?in_study_id - Microsoft Internet Explorer

Study Subject: Update

Date of Birth: 01/21/1973

Gender: Female

Subject: D1009

Race: NativeHawaiian/PacificIslander

Date of Consent: 07/09/2005

Removed from Study?

Class: Donor

Comment:

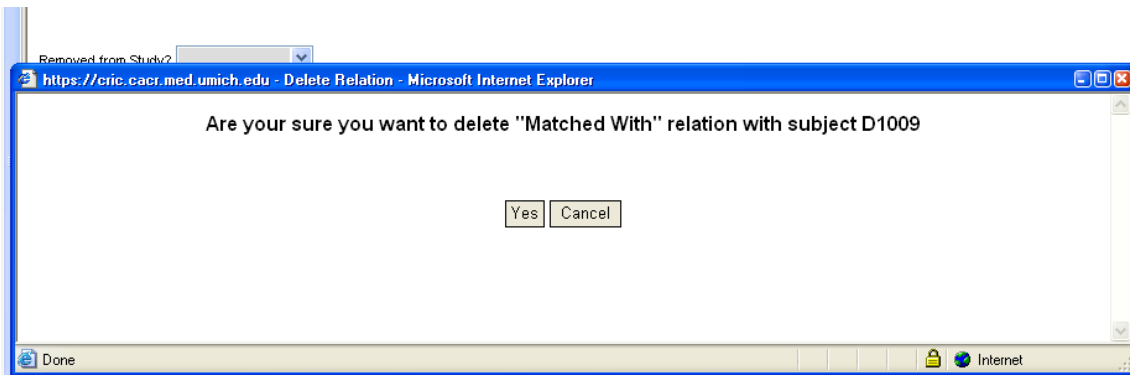
Subject Relationships

[Add a Relationship](#)

AKA A2LADR-R1735	
Matched With A2COH-D1009	Remove Relationship

Rejection
Hospitalization
Complication/Morbidity Event
Year 6 (Month 72)
Year 7 (Month 84)

9. If you've made an error and picked the wrong donor, you can correct it by clicking the "Remove Relationship" link on the Subject Relationships table. A new window will appear containing a confirmatory screen asking if you want to continue and delete the relationship between these two subjects. Click "Yes" to remove the relationship or "Cancel" to leave it as is.
 - The only reason to remove a relationship once you've associated the recipient and a donor is if you've made a mistake. Do not remove a relationship if the donor ends up not donating or is removed from consideration as a donor in the future.



Subject Relationships

[Add a Relationship](#)

AKA A2LADR-R1735	
Matched With A2COH-D1009	Remove Relationship

10. If a recipient candidate has several donor candidates, you can enter multiple relationships between the recipient and his/her donors by following steps 1 through 7.

[Save](#) [Clear](#)

Subject Relationships

[Add a Relationship](#)

AKA A2LADR-R1735	
Matched With A2COH-D1009	Remove Relationship
Matched With A2COH-D1395	Remove Relationship



Prospective Cohort Data Entry Pages

Recipients Pre-TXP:

1. Recipient Demographics
2. Recipient Condition at Enrollment
3. Recipient Pre-TXP Quarterly Assessment
4. HCV Data at Enrollment
5. HCC Data at Enrollment
6. HCV Pre-TXP Quarterly Assessment
7. HCC Pre-TXP Quarterly Assessment
8. Recipient Hospitalizations (pre and post txp)

Recipients @ TXP:

1. Recipient Condition at TXP
2. Recipient Intraoperative Data
3. HCV Data at TXP
4. HCC Data at TXP
5. HCC Explant Assessment

Recipients Post-TXP

1. Recipient Condition at 1 Week Post-TXP
2. Recipient Condition at 2 Weeks Post-TXP
3. Recipient Condition at 1 Month Post-TXP
4. Recipient Condition at 3 Months Post-TXP
5. Recipient Condition at 6 Months Post-TXP
6. Recipient Condition at 1 Year Post-TXP
7. Recipient Condition at 2 Years Post-TXP
8. Recipient Condition at 3 Years Post-TXP
9. Recipient Condition at 4 Years Post-TXP
10. Recipient Condition at 5 Years Post-TXP
11. Recipient Morbidity/Complication Severity
12. Multiple Rejection Episodes and Treatment
13. HCV Data at 1 Week Post-TXP
14. HCV Data at 1 Month Post-TXP

15. HCV Data at 3 Months Post-TXP
16. HCV Data at 1 Year Post-TXP
17. HCV Data at 2 Years Post-TXP
18. HCV Data at 3 Years Post-TXP
19. HCC Data at 3 Months Post-TXP
20. HCC Data at 6 Months Post-TXP
21. HCC Data at 1 Year Post-TXP
22. HCC Data at 18 Months Post-TXP
23. HCC Data at 2 Years Post TXP
24. HCV Biopsy Pathology Report Form

Donors Pre-Donation:

1. Donor Demographics
2. Donor Evaluation
3. Donor Hospitalizations (pre & post donation)

Donors at Donation:

1. Donor Intraoperative Data

Donors Post Donation:

1. Donor Morbidity and Complication Severity
2. Donor Condition at 1 Week Post-Donation
3. Donor Condition at 1 Month Post-Donation
4. Donor Condition at 3 Months Post-Donation
5. Donor Condition at 1 Year Post-Donation
6. Donor Condition at 2 Years Post-Donation
7. Donor Condition at 3 Years Post-Donation
8. Donor Condition at 4 Years Post-Donation
9. Donor Condition at 5 Years Post-Donation

Misc.

1. Complication/Morbidity and AE/SAE Tracking
2. AE/SAE Report

2. DEFINITIONS OF RECIPIENT ADVERSE EVENTS

The following is a guide for identification of complications. In general adverse events that are considered to be a deviation from normal postoperative course and have required some type of intervention are considered as complications. Intervention is defined as a requirement of treatment by medications, endoscopic, radiologic, and/or surgical approaches. Endoscopic interventions are defined as endoscopic procedures that are performed for purposes other than diagnosis. These include procedures such as banding or injection of varices, placement of stents or dilatation of strictures, and/or drainage of collections. Intervention radiological procedures may include drainage of thoracic or abdominal collections, placements of drains, stents or dilatation of strictures and/ or embolization for bleeding. For all complications, the date of the event is recorded. The severity of the complication is also recorded as outlined in the severity grading system.

B. Biliary complications

B1. A bile leak is defined as a persistent bilious drainage beyond 7 days after surgery that may occur from the cut surface of the liver, from the donor's oversewn bile duct stump, or an unidentified accessory duct. The presence of bile leak is identified by the presence of bilious drainage beyond 7 days in the drain, outlined by a radiological study such as ERCP or transhepatic cholangiograph, or identified during surgical exploration. Additionally a bile leak may manifest as a fluid collection of bile (biloma), which is identified on CT scan and may require either radiological or surgical intervention.

B2. Biliary stricture: Presence of defined narrowing of the intrahepatic or extrahepatic bile ducts as radiologically identified by ERCP or transhepatic cholangiography. A bile stricture may occur at any time after donation.

C. Abdominal/ GI

C1. Intra-abdominal bleeding. Any bleeding within the abdomen. If a patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes only "one" episode. Also record the total number of packed red blood cell units transfused.

C2. GI Bleeding. Bleeding communicating with the GI tract. This may be originating from the upper (esophagus, stomach, duodenum) or lower (small intestine distal to the duodenum, colon or rectum). If a patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes only "one" episode. Also record the total number of packed red blood cell units transfused. The cause of GI bleeding should be also recorded.

C3. Localized intra-abdominal abscess/fluid. These are collection that contain pus and are accompanied by peritonitis and or manifestations of infection such as fever or elevated white count. They are identified by CT scan, ultrasonography or during reoperation and require treatment such as antibiotic therapy, surgical or radiological intervention. Clinically insignificant collections that are detected during routine radiological studies, but do not require treatment, should not be documented as complications. If an intrabdominal collection contains bile, it should be classified under B1, as a bile leak.

C4. Prolonged ileus. This is defined by delayed return of bowel function for > 7 days after surgery. This is manifested by the delay in oral intake, bowel movements, and/or prolonged nasogastric suctioning. Please record the length of ileus defined as the time from surgery to the day of resumed oral intake.

C5. Bowel obstruction. This is manifested by the delay in oral intake, bowel movements, and/or prolonged nasogastric suctioning beyond 7 days after the initial operation in the presence of radiological study documenting the absence of continuity of the GI tract. This may be treated by conservative measures (GI suctioning, IV fluids) or by surgical intervention.

C6. Re-exploration. This is defined as unplanned return to the operating room following the initial procedure. The findings during the second procedure should be documented as negative if the surgeon did not identify any findings that required additional treatment or surgical procedures. If findings were identified that required additional therapy or operative procedure, this exploration should be documented as a positive exploration. Findings of a positive exploration should be documented as an additional complication. Example: If a patient undergoes a laparotomy for increasing abdominal pain and no new findings were documented during this surgery, this is documented as a negative laparotomy. If a bile leak that requires additional surgery was encountered, this is documented as a positive laparotomy. Additional, a bile leak complication should be checked under B1. If an abscess is found, this is documented as a positive laparotomy and an additional complication is marked under C3.

D. Cardiopulmonary

1. Myocardial infarction. Interruption of the blood supply to an area of the myocardium causing necrosis. Diagnosis is made by new ST-segment elevation or Q waves on EKG or with a ratio of CKMB:CK ≥ 2.5 or elevated troponin levels.

2. Congestive Heart failure (CHF). The inability of the heart to maintain an adequate blood flow. This results in congestion of the blood in certain veins and organs with an inadequate blood supply to body tissues. Diagnosis is made by the presence of acute pulmonary edema or cardiomegaly on chest X-ray. If performed, an echocardiogram should demonstrate one or more of the following findings, depressed left or right ventricular systolic function on echocardiography, any regional wall motion abnormality, or left or right ventricular hypertrophy.

3. Pneumothorax. Air or gas in the pleural space. Document only those resulting in chest tube placement

4. Pleural effusion. Fluid in the pleural space. Pleural effusion is common in both living donors and recipients following donation or transplantation. Document only those resulting in chest tube placement or tapping of fluid.

5. Pulmonary edema. Accumulation of fluid in the interstitial lung tissues. Diagnosis is confirmed by a chest X-ray that is reported to show pulmonary edema, without other findings to suggest congestive heart failure (number 2).

6. Cardiopulmonary Arrest. A sudden cessation of the heart with lack of respiration. Document only complete cardiopulmonary arrests that require CPR. If CPR is not successful and the patient died, please complete a death form. If the patient suffered from a respiratory arrest that was not accompanied by cardiac arrhythmias or cardiac standstill, do not check here.

7. Respiratory Arrest. Respiratory arrest that required re-intubation and was not accompanied by cardiac arrhythmias or cardiac standstill. If CPR is not successful and the patient died, please complete a death form.

8. Aspiration. Aspiration of a sufficient volume of gastric acid produces a chemical pneumonitis with or without a secondary infection. Document the occurrence of sudden respiratory distress that may require intubation associated with the appearance of a new, focal infiltrate on a chest X-ray or suctioning of gastric contents from an endotracheal tube should intubation occur.

9. Pulmonary embolus. Patients should have sudden onset of dyspnea associated with tachypnea and tachycardia in the presence of a normal chest X-ray. Document those with a high probability for embolus V/Q scan or a spiral CT of the chest that demonstrates an embolus.

E. Wound Complications

19. Dehiscence

20. Hernia development

F. Liver specific events

Defined as events specifically related to the function of the liver. These events correlate with worsening liver function and should be recorded as yes or no.

1. Encephalopathy defined as liver-induced altered mental status or disturbed level of consciousness. This is based Definition based on diagnosis listed by examining physician, and treatment is required in form of lactulose, neomycin or metronidazole therapy. This category includes hepatic coma.

2. Ascites. Defined as the use of diuretics (typically furosemide, spironolactone, bumetanide or metalazone) or paracentesis to manage ascites. Physical examination or imaging study such as ultrasound/abdominal CT or MRI should describe free intraperitoneal fluid or presence of ascites.

3. Liver Failure. Defined as generalized deterioration of the hepatic function as manifested by the development of encephalopathy, renal insufficiency (serum creatinine >2), abnormal prothrombin time that is progressive and ultimately leads to listing for transplant.

4. Hepatic artery thrombosis. Defined as loss of flow in the hepatic artery as determined by ultrasonography, angiography, CT angiography or MRA or intraoperative assessment of vessel. This should be recorded even if it did not lead to retransplant.

5. Portal vein thrombosis as proven by ultrasonography, angiography, CT angiography or MRA or detected during a surgical procedure. . This should be recorded even if it did not lead to transplantation.

6. Primary graft non-function: Progressive worsening of liver function as measured by elevated prothrombin time, with no explanation on a technical basis (no vascular thrombosis by ultrasound), and need for re-transplant.

7. Retransplantation. Defined as having received a liver graft for liver failure. Cause or retransplantation should be recorded.

8. Acute rejection: Histologic evidence of features of rejection that lead to adjustment of immunosuppressive therapy or treatment with pulse steroids or antibody agents.

9. HCV recurrence: Histologic evidence of graft damage secondary to hepatitis C and evidence of viremia.

10. HCC recurrence: Imaging of lesion either within the liver or other extrahepatic site that is suspicious for recurrent or metastatic disease. Tissue diagnosis is not necessary.

11. Chronic rejection: Histologic evidence of features of chronic rejection. This process does not necessarily need to be treated to qualify as a complication.

G. General

1. Deep venous thrombosis. Presence of thrombosis of the lower extremities as verified by an imaging study such as ultrasound/Doppler with the requirement of post-operative anti-coagulation therapy.

2. Neuropraxia. Sensory or motor peripheral nerve dysfunction that results in altered sensations or loss of motor function in the absence of a central nervous system disorder. This mostly occurs in the upper extremity, but can also occur in lower extremity.

3. Infections. Defined in general as a body fluid or tissue sample with a positive laboratory culture result that is treated with an intervention. This may include hospitalization, antibiotics, bedside wound opening, or formal surgical intervention. Exceptions to a positive culture are noted below. In addition to whether infection was present, the specific site should be recorded using the definitions below:

Wound: Surgical wound infection or deep intrabdominal abscess which requires intervention

Biliary Tree: Episode of cholangitis defined as blood borne organisms, which are cultured in the setting of abnormal liver function tests or imaging study revealing biliary tract disease. Also included is fluid collection, which contain bile and are believed to be in communication with the biliary tree.

Blood: Blood borne organism is cultured with no other defined source. This would include bacteria or fungemia presumed secondary to an indwelling line infection

Liver: Intrahepatic fluid collections, which are determined to be an abscess, as evidenced by positive culture of aspirated or drained fluid.

Pulmonary: Diagnosis is made by the presence of new or progressive focal pulmonary infiltrates on chest x-ray or CT scan and some degree of pulmonary compromise (clinical symptoms of shortness of breath, signs of tachypnea, abnormal blood gas, ventilator requirement) and may be accompanied by purulent tracheobronchial secretions, fever, leukocytosis, and/or a positive culture from sputum. A positive culture is not needed for this type of infection.

CNS: Mental status changes or neurologic findings and an abnormal exam of cerebral spinal fluid. In the case of fungal infection, characteristic mass lesions on imaging are adequate.

Urinary tract: Urine is culture positive for an organism and treatment is started.

H. Other Complications

This includes complications that were not outlined in the above categories that have required intervention.

DEFINITIONS OF DONOR COMPLICATIONS/MORBIDITY EVENTS

The following is a guide for identification of complications. In general adverse events that are considered to be a deviation from normal postoperative course and have required some type of intervention are considered as complications. Intervention is defined as a requirement of treatment by medications, endoscopic, radiologic, and/or surgical approaches. Endoscopic interventions are defined as endoscopic procedures that are performed for purposes other than diagnosis. These include procedures such as banding or injection of varices, placement of stents or dilatation of strictures, and/or drainage of collections. Intervention radiological procedures may include drainage of thoracic or abdominal collections, placements of drains, stents or dilatation of strictures and/ or embolization for bleeding. For all complications, the date of the event is recorded. The severity of the complication is also recorded as outlined in the severity grading system.

A. Intraoperative Injury

These are injuries that occur during the operative procedure and refer to the donor structures. If a right hepatectomy procedure is performed any injury to the donor structures, namely the common bile duct, the left hepatic duct, the left hepatic artery, common hepatic artery, left branch of the portal vein, and the main trunk of the portal vein should be recorded. If a left lobe hepatectomy is performed, injury to the common bile duct, the right hepatic duct, the right hepatic artery, common hepatic artery, right branch of the portal vein, and the main trunk of the portal vein should be recorded.

Injury to these structures may be detected and reported at the time of the primary operation or documented by diagnostic testing or surgical re-exploration during hospitalization. For example, an injury to the bile duct may manifest as a persistent bile duct leak in the post-operative period that is detected by ERCP or a bile leak that requires surgical exploration, repair or drainage. Donor hepatic arterial injury may be detected during the initial procedure or manifest by donor arterial thrombosis, bleeding, or pseudoaneurysm formation as evidenced by a doppler study, hepatic angiography, or CT angiography. Portal vein injuries may be manifested by bleeding in the primary procedure, or by portal vein thrombosis as documented postoperatively by a doppler study, hepatic angiography, or CT angiography.

B. Biliary complications

B1. A bile leak is defined as a persistent bilious drainage beyond 7 days after surgery that may occur from the cut surface of the liver, from the donor's oversewn bile duct stump, or an unidentified accessory duct. The presence of bile leak is identified by the presence of bilious drainage beyond 7 days in the drain, outlined by a radiological study such as ERCP or transhepatic cholangiograph, or identified during surgical exploration. Additionally a bile leak may manifest as a fluid collection of bile (biloma), which is identified on CT scan and may require either radiological or surgical intervention.

B2. Biliary stricture: Presence of defined narrowing of the intrahepatic or extrahepatic bile ducts as radiologically identified by ERCP or transhepatic cholangiography. A bile stricture may occur at any time after donation.

C. Abdominal/ GI

C1. Intra-abdominal bleeding. Any bleeding within the abdomen. If a patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes only "one" episode. Also record the total number of packed red blood cell units transfused.

C2. GI Bleeding. Bleeding communicating with the GI tract. This may be originating from the upper (esophagus, stomach, duodenum) or lower (small intestine distal to the duodenum, colon or rectum). If a patient experiences a series of bleeds over several days, but never fully

recovers between them, this constitutes only “one” episode. Also record the total number of packed red blood cell units transfused. The cause of GI bleeding should be also recorded.

C3. Localized intra-abdominal abscess/fluid. These are collection that contain pus and are accompanied by peritonitis and or manifestations of infection such as fever or elevated white count. They are identified by CT scan, ultrasonography or during reoperation and require treatment such as antibiotic therapy, surgical or radiologic intervention. Clinically insignificant collections that are detected during routine radiologic studies, but do not require treatment, should not be documented as complications. If an intra-abdominal collection contains bile, it should be classified under B1, as a bile leak.

C4. Prolonged ileus. This is defined by delayed return of bowel function for > 7 days after surgery. This is manifested by the delay in oral intake, bowel movements, and/or prolonged nasogastric suctioning. Please record the length of ileus defined as the time from surgery to the day of resumed oral intake.

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and the patient died, please complete a death form. If the patient suffered from a respiratory arrest that was not accompanied by cardiac arrhythmias or cardiac standstill, do not check here.

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3. Liver Failure. Defined as generalized deterioration of the hepatic function as manifested by the development of encephalopathy, renal insufficiency (serum creatinine >2), abnormal prothrombin time that is progressive and ultimately leads to listing for transplant.

4. Hepatic artery thrombosis. Defined as loss of flow in the hepatic artery as determined by ultrasonography, angiography, CT angiography or MRA or intraoperative assessment of vessel. This should be recorded even if it did not lead to transplantation.

5. Portal vein thrombosis as proven by ultrasonography, angiography, CT angiography or MRA or detected during a surgical procedure. . This should be recorded even if it did not lead to transplantation.

6. Inferior vena caval thrombosis as proven by ultrasonography, angiography, CT angiography or MRA or detected during a surgical procedure.

7. Transplantation. Defined as having received a liver graft for liver failure.

G. General

1. Deep venous thrombosis. Presence of thrombosis of the lower extremities as verified by an imaging study such as ultrasound/Doppler with the requirement of post-operative anti-coagulation therapy.

2. Neuropraxia. Sensory or motor peripheral nerve dysfunction that results in altered sensations or loss of motor function in the absence of a central nervous system disorder. This mostly occurs in the upper extremity, but can also occur in lower extremity.

3. Infections. Defined in general as a body fluid or tissue sample with a positive laboratory culture result that is treated with an intervention. This may include hospitalization,

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CNS: Mental status changes or neurologic findings and an abnormal exam of cerebral spinal fluid. In the case of fungal infection, characteristic mass lesions on imaging are adequate.

Urinary tract: Urine is culture positive for an organism and treatment is started.

4. Psychological. Major psychological issues that have required treatment or hospitalizations such as depression or suicidal attempts.

H. Other Complications

This includes complications that were not outlined in the above categories that have required intervention.

Assembling the A2ALL Ambient Shipper

1. For vials of tissue preserved in formalin:

Place up to 81 x 2ml vials in the specimen box.

For tissue blocks:

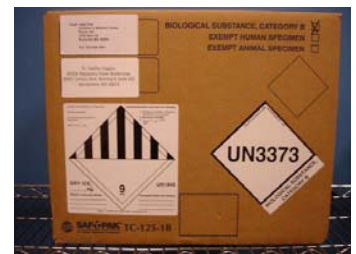
Six cell divider walls may be removed from the specimen box so that 27 tissue blocks will fit in the box (i.e., 9 across, 3 down). A cell divider also may be removed completely if tissue blocks are placed inside a sealed bag, in the specimen box.

2. Place the specimen box inside the leak-proof plastic bag. When shipping tissue in formalin, place an absorbent sheet inside the bag. Remove the strip of paper covering the adhesive and seal the bag.
3. Place the plastic bag inside the white Tyvek envelope; remove the strip of paper covering the adhesive on the flap and seal the envelope.
4. Place the Tyvek envelope in the insulated shipping container. Fill any empty space inside the container with bubble wrap to prevent shifting during shipment.
5. Place the styrofoam lid on the cooler. Place a copy of the shipping log on top of the styrofoam lid.
6. Close and tape the outer cardboard box.
7. Affix the repository address label to the top of the box in the upper right corner.
8. Affix the "Exempt Human Specimen" label to the top of the box below the repository address label.
9. Use the pre-printed Fed Ex air bill to ship the specimens to the NIDDK Biosample Repository.
 - a. In Section 1, fill in your name, return address, phone number, and date. (Leave "Sender's FedEx account number" blank.)
 - b. In Section 6, check the "No" block indicating no dangerous goods are contained in the shipment.
 - c. In Section 7, enter "1" under "Total Packages", and the total weight of the package. The package should weigh approximately 2 - 3 pounds.
10. Follow the peel-and-stick instructions on the back of the air bill. As shown, affix the air bill to the side of the box.
11. Call Federal Express at 1-800-GO-FEDEX (1-800-463-3339). Give them the account number on the preprinted FedEx air bill (in Section 7, Payment) and your pickup address. FedEx will dispatch a courier to pick up the package. Please schedule shipments Monday through Wednesday to avoid weekend shipment delays. **Do not ship samples on Friday; the repository is closed on weekends.**
12. Send a shipment notification to the repository via email at BIO-NIDDKRepository@thermofisher.com on the day the package is picked up by FedEx. Include the 12-digit FedEx tracking number in the notification.
12. Contact the NIDDK Repository via email or call Heather Higgins (240-793-0353) or Sandra Ke (240-686-4702) regarding questions about packaging and shipping.



Assembling the STP 320 Repository Shipper

1. Upon receipt of the empty shipping kit from the NIDDK Biosample Repository, remove the "EMPTY PACKAGING" cardboard piece from the outer box.
2. Place up to 81 x 2ml cryovials in each specimen box. Place each specimen box and an absorbent sheet inside a plastic biohazard bag. Seal the bag.
3. Place each plastic biohazard bag inside a white Tyvek envelope. Seal the envelope.
4. Place the Tyvek envelopes in the cardboard inner box. If only one or two specimen boxes are being shipped, fill the rest of the space inside the cardboard inner box with packing material (e.g., bubble wrap) or an empty specimen box to prevent movement during shipment. Close and tape the inner cardboard box and set it in the middle of the cooler.
5. Completely fill the space between the inner cardboard box and the inner walls of the cooler with dry ice.
6. Place the lid on the cooler. Place the "EMPTY PACKAGING" cover and shipping log on top of the cooler lid.
7. Close and tape the outer cardboard box.
8. Place a checkmark in the block on the outer cardboard box next to "BIOLOGICAL SUBSTANCE, CATEGORY B". Do not cover this marking with labels.
9. Affix a label with your name and return address to the side of the box in the "Shipper:" block.
10. Affix the repository address label to the side of the box in the "Consignee:" block.
11. Affix the dry ice label below the repository address label. Enter the weight of dry ice on the label in kilograms.
12. Affix the "UN3373 BIOLOGICAL SUBSTANCE, CATEGORY B" label to the right of the dry ice label.
13. Use the pre-printed Fed Ex air bill to ship specimens to the NIDDK Repository:
 - a. Section 1: Fill in your name, return address, phone number and the date. Leave "Sender's FedEx Account Number" blank.
 - b. Section 6, Special Handling: Check "Yes, Shippers Declaration not required". Check the "Dry Ice" block; enter "1" and the weight of dry ice in kg.
 - c. Section 7: Enter "1" under "Total Packages" and the total weight of the package.
 - d. Follow the peel-and-stick instructions on the back of the air bill. As shown, affix the air bill to the side of the box adjacent to the labeled side.
14. Call Federal Express at 1-800-GO-FEDEX (1-800-463-3339). Give them the account number on the preprinted FedEx air bill (in Section 7, Payment) and your pickup address. FedEx will dispatch a courier to pick up the package. Please schedule shipments Monday through Wednesday to avoid weekend shipment delays. **Do not ship samples on Friday; the repository is closed on weekends.**
15. Send a shipment notification to the repository via email at BIO-NIDDKRepository@thermofisher.com on the day the package is picked up by FedEx. Include the 12-digit FedEx tracking number in the notification.
16. Contact the NIDDK Biosample Repository via email or call Heather Higgins (240-793-0353) or Sandra Ke (240-686-4702) regarding questions about packaging and shipping.





Collecting Samples

1. Collect the appropriate samples from the patient for that time point, and if necessary, aliquot and place in the appropriate storage vials.
2. Affix label to sample vials
3. One bar code id sample to each vial
4. There is a unique value for each planned sample that goes to Fisher (formerly McKesson). The 3 tubes of blood for the Genetics Repository all have the same Sample ID.
5. Click the link to the Sample Processor in the Study Programs area of BioDBx:

Current User: Joe Bonner [Logout]
 Current Study: A2COH
 Current Site:

Study Programs:

Demo Web Pages:

6. In the “Action” box, choose “Log Samples”, then click the “Continue” button

Site: <input type="text" value="Test"/>	Action: <input type="text" value="Log Samples"/>
<input type="button" value="Continue"/>	<input type="button" value="Continue"/>

7. Scan the bar code for the first sample. Hit the “Tab” key and enter the date of collection (MM/DD/YYYY). The rest of the fields will prepopulate. Click the “Insert” button. On the lower left, you will see a “Success” message that tells you that you have successfully entered that sample.

Site: <input type="text" value="Test"/>	Action: <input type="text" value="Log Samples"/>
<input type="button" value="Continue"/>	<input type="button" value="Continue"/>

Sample ID	Collected On	Site Label	Subject Label	Sample Label	
18918	09/23/2004	T	T1130	Aliquot - 1	Seru
18919	09/23/2004	T	T1130	Aliquot - 2	Seru
18916	09/23/2004	T	T1130		Who

Success

- 8. Continue scanning and entering samples until you have entered all of the samples you have collected. When you are done inserting the last sample (make sure you click “Insert” for that last sample), Click the “Log Samples” button. You will see a confirmation screen telling you that the samples’ status has changed from “Pending” to “Collected”

Site: Test <input type="button" value="Continue"/>	Action: Log Samples <input type="button" value="Continue"/>	
Your Samples have been added to the Log and their status has been updated to Colected		
Click Here To Return Home		



Declaring a Visit in BioDBx

Once you know the date the next visit is scheduled, declare the visit for subject.

YOU MUST DECLARE THE VISIT OR NONE OF THE SUBJECT AND SAMPLE REPORTS WILL WORK PROPERLY!

1. Scroll down on the PHI page to the “Contact” window.

BioDBx Main Page

Show All Subjects Search for Subject

Current User: Peg Hill-Callahan [Logout]
 Current Study: A2LADR
 Current Site: Colorado - Colorado
 Study Programs:
 Demo Web Pages

Current Subject: R1463

- Enter Data
- Baseline/Screening
- Treatment/Randomization
- vWeek 1
- vWeek 2
- vWeek 3
- vWeek 4
- vWeek 6
- vWeek 8
- vWeek 10
- vWeek 12
- vWeek 16
- vWeek 20
- vWeek 24
- vWeek 28
- vWeek 32
- vWeek 36
- vWeek 40
- vWeek 44
- vWeek 48
- Txp/Dntn Surg
- vWeek 12 Post TXP
- vWeek 24 Post TXP

Save Clear

Contact for R1463

[Add a Contact](#) | [Close the Window](#)

Contact No.	Contact Date	Contact Type	Made By	Comment	Samples	Actions
		Week 4			To Samples	Update/Remove Enter Data
		Week 8			To Samples	Update/Remove Enter Data
		Week 12			To Samples	Update/Remove Enter Data
		Week 24			To Samples	Update/Remove Enter Data
		Week 48			To Samples	Update/Remove Enter Data

2. Check to see if the visit is on the table. If it isn't, click the “Add a Contact” button. Choose the contact type from the drop down box. Select your name from the “Contact Made By” drop down box. The Date/Time will be automatically populated with today's date. If the contact isn't occurring on today's date, select over the date and enter the correct one.

Add a New Contact for A2LADR-Colorado R1463

Contact Type* -- Select Contact Type --

Contact Made By -- Select Contact Type --

Date/Time* (format: mm/dd/yyyy)

Comment

Note: * fields value required.

- Baseline/Screening
- Treatment/Randomization
- Week 1
- Week 2
- Week 3
- Week 6
- Week 10
- Week 16
- Week 20
- Week 28
- Week 32
- Week 36
- Week 40
- Week 44
- Txp/Dntn Surg
- Week 48 Post TXP
- Complication/Morbidity Event
- AE/SAE
- Drug Accountability Logs

- Click the “Insert New Contact” button.

Add a New Contact for A2LADR-Colorado R1463

Contact Type* Baseline/Screening


Contact Made By Peg Hill-Callahan

Date/Time* 07/25/2005
(format: mm/dd/yyyy)

Comment

Note: * fields value required.

- Scroll down to the bottom of the PHI page and note that your new contact has been added to the table.



Main Page

Current User: Peg Hill-Callahan [Logout]
 Current Study: A2LADR
 Current Site: Colorado - Colorado
 Study Programs:
 Demo Web Pages

Current Subject: R1463

- Enter Data
- Baseline/Screening
- Treatment/Randomization
- Week 1
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- Week 48
- Txp:Intr Surg
- Week 12 Post TXP
- Week 24 Post TXP
- Week 48 Post TXP

Removed from Study* ▼

Class: Recipient

Contact for R1463

[Add a Contact](#) | [Close the Window](#)

Contact No.	Contact Date	Contact Type	Made By	Comment	Samples	Actions
9	07/25/2005	Baseline/Screening	PEGHC		To Samples	Update/Remove Enter Data
		Week 4			To Samples	Update/Remove Enter Data

- If the study visit is already on the Contact Table, you will need to associate a date with the study visit. Click the “Update/Remove” link.

- Week 4
- Week 6
- Week 8
- Week 10
- Week 12
- Week 16
- Week 20
- Week 24
- Week 28
- Week 32
- Week 36
- Week 40
- Week 44
- Week 48
- Txp:Intr Surg
- Week 12 Post TXP
- Week 24 Post TXP

Contact for R1463

[Add a Contact](#) | [Close the Window](#)

Contact No.	Contact Date	Contact Type	Made By	Comment	Samples	Actions
		Week 4			To Samples	Update/Remove Enter Data
		Week 8			To Samples	Update/Remove Enter Data
		Week 12			To Samples	Update/Remove Enter Data
		Week 24			To Samples	Update/Remove Enter Data
		Week 48			To Samples	Update/Remove Enter Data

- The contact type will be pre-populated. Don't change it. Select your name from the drop-down list, and enter the date of the visit. The date does not prepopulate. Add a comment if you wish to. Click the "Update/Remove Contact" button.

Update/Remove Contact for A2LADR-R1463

Contact Type: Week 4

Contact Made By: Peg Hill-Callahan

Contact Date * 07/25/2025
(format: mm/dd/yyyy)

Comment: Subject declined to have blood drawn.

Remove:

Update/Remove Contact
Cancel the Changes
Close

Note: * fields value required.

- Scroll down on the PHI page and note that the contact has been updated with the date, the person declaring the contact, and any comments.

Current Subject: R1463

- Enter Data
- Baseline/Screening
- Treatment/Randomization
- Week 1
- Week 2
- Week 3
- Week 4
- Week 6
- Week 8
- Week 10
- Week 12
- Week 16
- Week 20
- Week 24
- Week 28
- Week 32
- Week 36
- Week 40
- Week 44
- Week 48

[Save](#) [Clear](#)

Contact for R1463

[Add a Contact](#) | [Close the Window](#)

Contact No.	Contact Date	Contact Type	Made By	Comment	Samples	Actions
9	07/25/2005	Baseline/Screening	PEGHC		To Samples	Update/Remove Enter Data
10	07/25/2005	Treatment/Randomization	PEGHC		To Samples	Update/Remove Enter Data
	07/25/2025	Week 4	PEGHC	Subject declined to have blood drawn.	To Samples	Update/Remove Enter Data
		Week 8			To Samples	Update/Remove Enter Data

- Click the "Enter Data" link and begin entering data. The folder structure will contain the date of the contact and will collapse and show only the folders appropriate to this study time point. Click the icon next to the form on which you want to enter data. To update other future contacts, you can access the "Update/Remove Contact" menu by searching for the subject and clicking on the "PHI" button.

Main Page

[Show All Subjects](#)

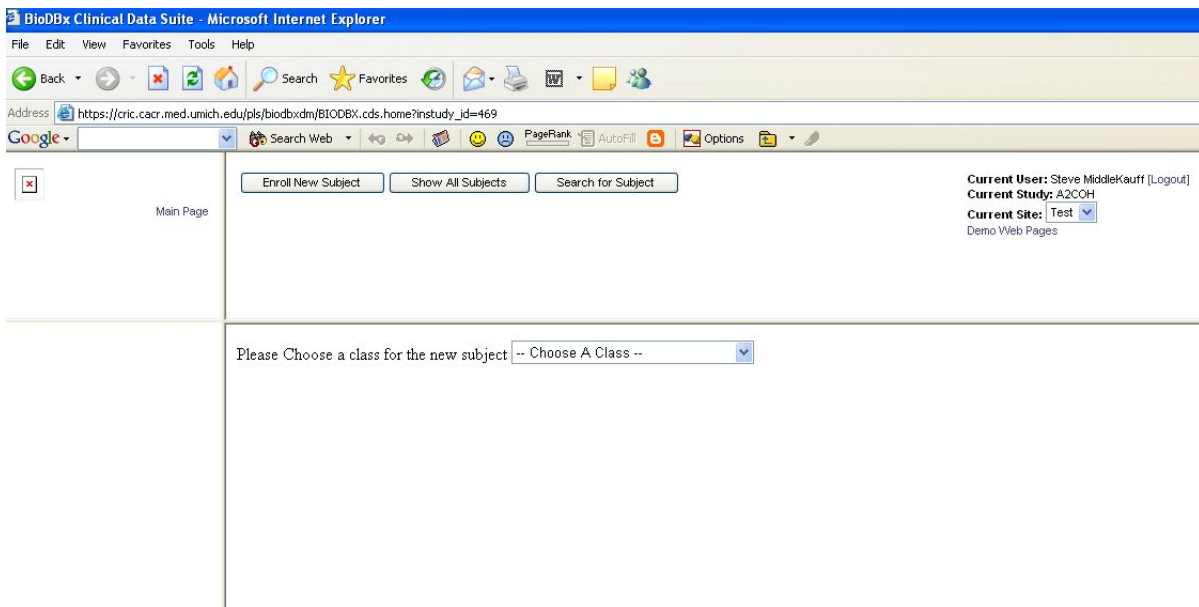
Current Subject: R1463

- Enter Data
- Week 4 07-25-2025
- AE/SAE
- Drug Accountability Logs

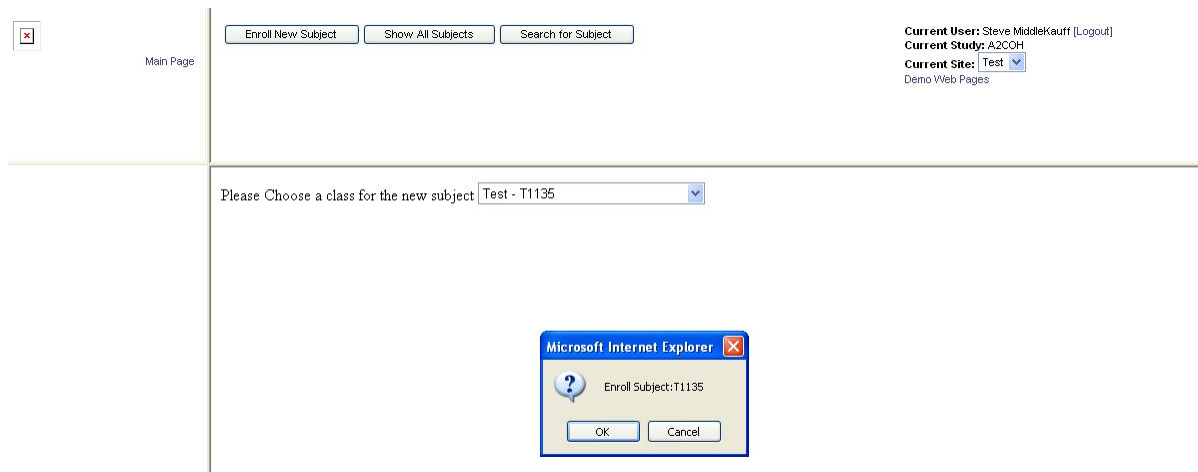


Enrolling Subjects in BioDBx

1. Click the Enroll New Subject button
2. Choose the class for your new subject (Donor or Recipient)
 - a. Note: Recipients must be entered first because you'll need their Subject Label on the Donor enrollment so we can link the two subjects.



3. BioDBx will assign the next available subject number to your new enrollee.
 - a. You'll be prompted to ensure that you want to enroll the selected subject. Click "OK"



- b. Enter data on the new page
 - c. If you are not entering any contacts for the subject at this time, click the “save” button.
 - d. Copy down the subject’s BioDBx ID number.
4. Locate the pre-printed labels that the DCC sent to your site. Choose the batch of labels that correspond to the subject’s BioDBx number. Put those labels in a location where you can access them for the rest of the study.
5. If you are seeing the patient on the day you are enrolling, or if you know the date the next visit is scheduled, declare the visit for subject
 - a. Scroll down on the page to the “Contact” window.
 - b. Click on “add a contact”. A dialogue box will pop up prompting you to add a new contact. Choose the time point from the drop down box. The date and “contact made by” fields will be automatically populated. The date will be populated with the today’s date. If the patient is being seen on a future date, enter that date over today’s date. If you have any comments you’d like to make, enter them in the box.
 - c. Click the “Insert New Contact” Button. Your new contact will be added and the screen will go back to the Study Enrollment page.
 - d. Click “Save”

Current User: Steve MiddleKauff [Logout]
 Current Study: A2COH
 Current Site:
 Demo Web Pages

Label	Last Name	First Name	Med. Rec. No.	Samples	Enter Data	View Data	Discrepancies	Edit Data	View PHI
T1136				3	22				PHI

6. You can now choose to enter data for this subject by clicking the “Enter Data” button.
7. To add new or future contacts, you can access the “Add a Contact” menu by searching for the subject and clicking on the “PHI” button.



Other Reporting Functionality

1. In addition to viewing sample status at a site-specific level you can also view sample and form status on a subject level.
2. Click on the “Subject Status Report” in the drop-down box next to the subject’s PHI button

Enroll New Subject Show All Subjects Search for Subject

Current User: Peg Hill-Callahan [Logout]
 Current Study: A2COH
 Current Site: Northwestern - Northwestern
 Study Programs: Sample Tracker
 Demo Web Pages

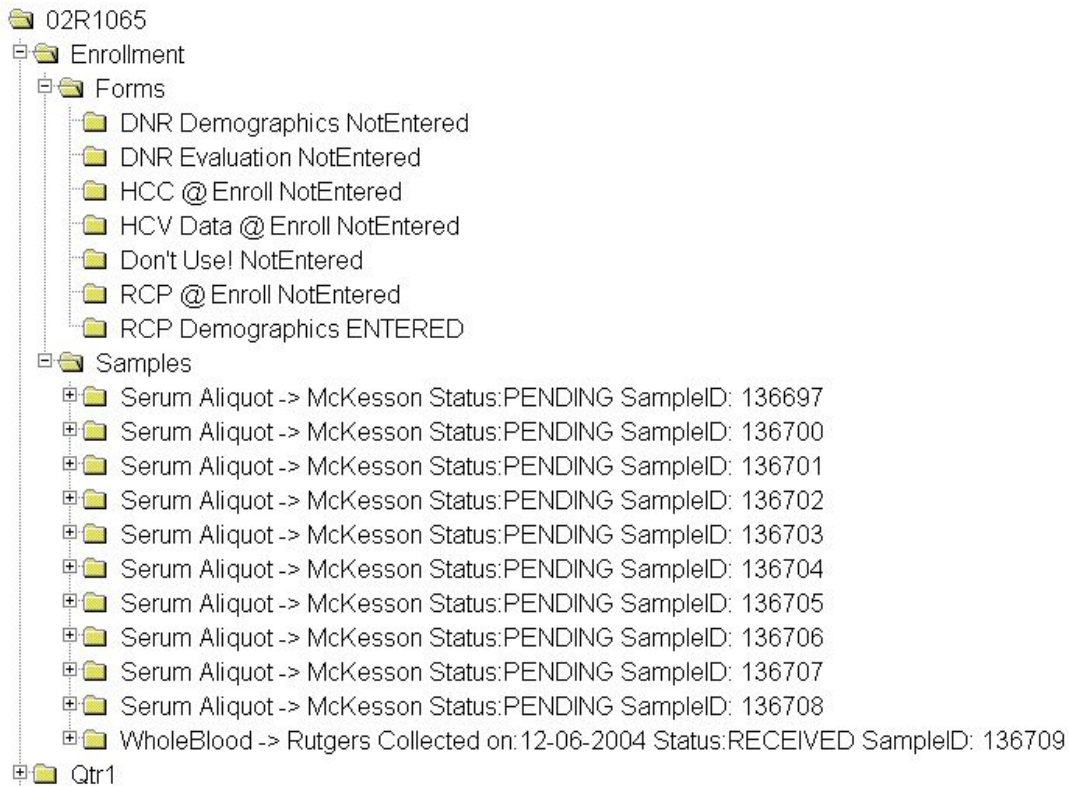
Label	Last Name	First Name	Med. Rec. No.	Samples	Enter Data	View Data	Discrepancies	Edit Data	View PHI
R1106				247	128	2			PHI

Subject Status Report

3. A new window will open up showing you the subject’s site and ID number with a series of folders and associated dates. Click on the “+” next to the time point for which you want to review the status of forms and samples.

- 02R1106
 - Enrollment 02-01-2005
 - Forms
 - Samples
 - Qtr1
 - Qtr2
 - Qtr3
 - Qtr4
 - Qtr5
 - Txp/Dntrn Surg
 - Day 1
 - Week 1
 - Week 2
 - Month 1
 - Month 3
 - Month 6
 - Month 12
 - Month 24
 - Month 36
 - Month 48
 - Month 60
 - Rejection
 - HCV Recurrence

4. Open the Forms or Samples folder and you can see the status of the pertinent items. Forms are shown as either NotEntered or ENTERED. Sample status is either: Pending, Collected, Shipped or Received:





Printing Bar Codes on Standard Paper

1. Install the font from the DCC.
 - a. Drag it from your email to your desktop and open up your Control Panel.
 - b. Click on Fonts.
 - c. In the file menu, click on “Install New Font”, and point the destination at your desktop where the font is located.
 - d. Alternatively, you can copy the font to your clipboard by highlighting it, holding your “Control” Key and the “C” key down at the same time.
 - e. Open your Control Panel and Font folder and hold your “Control” key and the “V” key down at the same time. This will paste the font into the proper folder. You may need to ask your IT staff for help if you don’t have install privileges on your computer.
2. You may print an 8.5” X 11” page of bar codes that correspond to the labels for all of the subjects for whom you’ve declared a visit. These are for use when scanning the actual samples’ bar codes into the system isn’t convenient or feasible (i.e. the samples are in the clinic area and you are updating sample collection at your computer in your office).
3. In BioDBx, click on the Sample Tracker program in the Study Programs window on the upper right side of your screen.



4. Choose your site.
5. Click on the folder that correlates to the collection date of the samples.
6. Click on Pending Samples.
- 7. Scroll Down**
8. Click on Print This Report
9. Note that the report is by Site. So, you will be viewing all samples that you are expecting to collect from visits you have declared. This may involve multiple subjects and time points.

10. You can also see what samples have been received by choosing that report. There will be a delay in seeing what is received since the repository only reports this information to the DCC every two weeks.

Please Choose a site

Sample Processing Report for A2COH (T) 02-Feb-2005 15:46:08


- This Week (30-Jan-2005 - 05-Feb-2005)
 - Samples: COLLECTED
 - Samples: PENDING
 - Samples: RECEIVED
 - Samples: SHIPPED
- Past Weeks
- Future Weeks

A2COH Sample Processing Report for Northwestern 02

Samples: PENDING for the week beginning 30-Jan-2005

Report run on 02-Feb-2005 15:46:35

Subject	Sample Status	Type	Date	Contact
R1106	PENDING	Serum Aliquot	Enrollment	-> McKesson



* 1 6 0 5 8 1 *

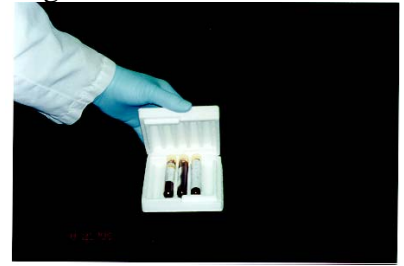
Feb. 2, 2005

ASSEMBLY INSTRUCTIONS FOR INTERNATIONAL POLYFOAM MAILERS

READ ALL INSTRUCTIONS THOROUGHLY BEFORE STARTING ASSEMBLY

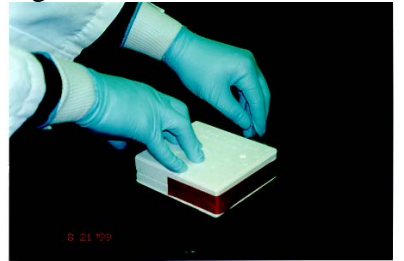
- 1) Place the labeled tubes into the small Styrofoam insert using the same insert that the empty tubes came in (Fig. 1). DO NOT tape the top of the blood tubes.

Fig. 1



- 2) Tape the small Styrofoam insert closed. Peel the backing from one piece of red waterproof tape and begin sealing the Styrofoam lid to the body. Then peel the backing from the second piece of tape and continue sealing the insert, overlapping the first piece of tape about two inches on both ends (Fig. 2).

Fig. 2



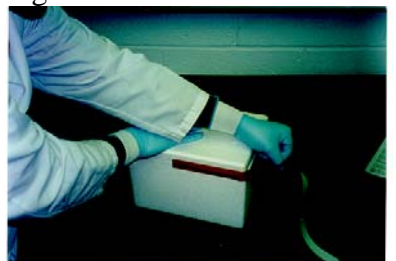
- 3) Place the small Styrofoam insert into the press-lock plastic bag. Seal the bag and place it into the large Styrofoam mailer (Fig. 3). Fill the mailer with packing material to prevent disturbing the blood tubes during shipment. Include a copy of the completed Data Collection Form inside the large Styrofoam mailer.

Fig. 3



- 4) Tape the large Styrofoam mailer closed. Peel the backing from one piece of red waterproof tape and begin sealing the Styrofoam lid to the body. Then peel the backing from the second piece of tape and continue sealing the mailer, overlapping the first piece of tape about two inches on both ends (Fig. 4).

Fig. 4



- 5) Slide the Styrofoam mailer into the corrugated carton (Fig. 5) and seal the carton with packing tape. Place the Federal Express International shipping form and any other necessary documents (i.e. International Invoice Form and Declaration Statement on Rutgers letterhead) on the outside of the carton and contact Federal Express FOR PICKUP.

Fig. 5



Assembly instructions for one Polyfoam Packers Model 472 Thermo~~is~~safe® Safety Mailer System

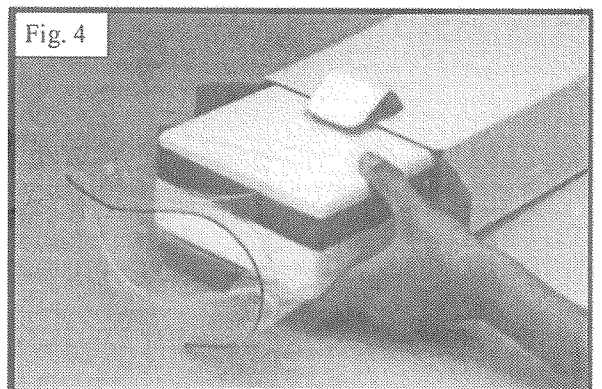
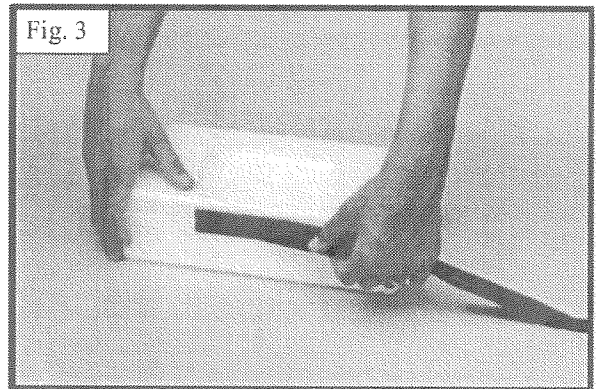
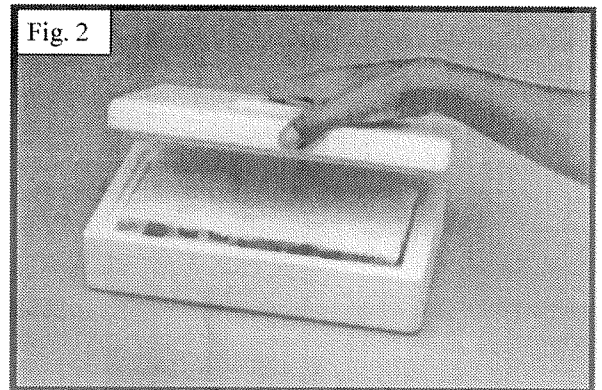
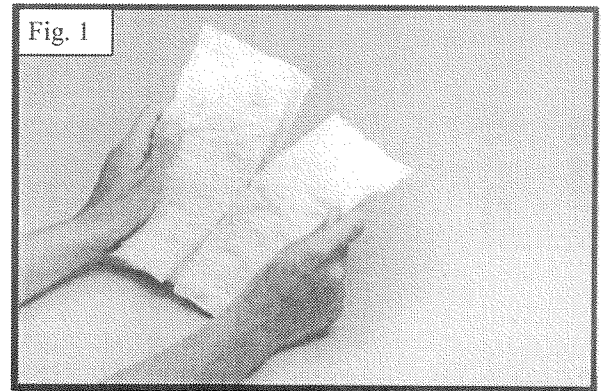
Read all instructions thoroughly before starting assembly.

Required Components:

- One Model 470 Safety Mailer (body and lid)
- One 2-1/2" x 9" pre-cut section of absorbent material
- One roll waterproof tape
- One press-lock plastic bag
- One corrugated shipping carton with locking tabs

Assembly Procedure:

- 1) Place tubes and other diagnostic test components in body of the Safety Mailer, as usual.
- 2) Tear off one section of absorbent material along the perforations (Fig. 1) and place it so it exactly covers the cavity of the Safety Mailer, including all diagnostic test components (Fig. 2).
- 3) Place the lid of the Safety Mailer over the body and absorbent material (Fig. 2), and press down firmly until the sides of the lid meet the sides of the body.
NOTE: If absorbent material is pinched between the lid and the body, the lid will not close properly. In this case, reposition absorbent material and then refit the Safety Mailer lid.
- 4) Cut two 18" long pieces of red, waterproof tape. Peel the backing from one piece of tape and begin sealing the Safety Mailer lid to the body (Fig. 3). Then peel the backing from the second piece of tape and continue sealing the mailer, overlapping the first piece of tape about two inches on both ends.
- 5) Place the sealed Safety Mailer into the press-lock plastic bag. **DO NOT SEAL THE BAG YET** (air trapped in the sealed bag will prevent it from fitting into the corrugated shipping carton).
- 6) Slide the Safety Mailer and open press-lock bag into the corrugated carton (Fig. 4). Then seal the press-lock bag, close the carton using the locking tabs, and place sealing tape (not included) over them.



POLYFOAM Packers

Division of Tuscarora Incorporated
Part of SCA Global Packaging

2320 Foster Ave, Wheeling, IL 60090-6572
800-323-7442 • 847-632-9600 • FAX 847-398-0653

www.polyfoam.com

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LIT 127-08/02



Shipping in BioDBx

1. Click the link to the Sample Processor in the Study Programs area of BioDBx

Current User: Joe Bonner [Logout]
 Current Study: A2COH
 Current Site: Test
 Study Programs:
 Demo Web Pages:

2. Choose “Prepare Shipment” action. Click “Continue”

Site: Test <input type="button" value="Continue"/>	Action: Prepare Shipment <input type="button" value="Continue"/>	
---	---	--

3. Choose “To Rutgers”(for whole blood to the Genetics Respository), “To McKesson” (for paraffin block liver Bx specimens), or “To McKesson Cold” (for frozen serum aliquots and frozen liver Bx specimens in RNALater), then click “Continue”.

Site: Test <input type="button" value="Continue"/>	Action: Prepare Shipment <input type="button" value="Continue"/>	Select Action: To McKesson <input type="button" value="Continue"/>
---	---	---

4. A list of collected samples available to ship to the selected repository will appear. Verify that samples listed are the samples you are ready to ship.
 - a. To remove from list samples that are not ready to be shipped, check the box next to each sample to be removed from the manifest and click “Remove Checked Samples”. Those samples will be deleted from that list and their status will be retained as “collected”.

Site: Test <input type="button" value="Continue"/>				
Sample ID	Collected On	Site Label	Subject Label	Sample Label
<input type="checkbox"/> 366312		T	T1766	Post-TXP/Donation
<input type="checkbox"/> 366315		T	T1766	Post-TXP/Donation
<input type="checkbox"/> 366317		T	T1766	Post-TXP/Donation
<input type="checkbox"/> 366319		T	T1766	Post-TXP/Donation
<input type="checkbox"/> 366321		T	T1766	Post-TXP/Donation
<input type="checkbox"/> 366323		T	T1766	Post-TXP/Donation
<input type="checkbox"/> 366325		T	T1766	Post-TXP/Donation
<input type="checkbox"/> 397144	4/19/2007 0:0:0	T	R1837	-> McKesson
<input type="button" value="Check all boxes"/>	<input type="button" value="Remove Checked Samples"/>	<input type="button" value="Ship"/>	<input type="button" value="Print"/>	

5. When the list is accurate, print the manifest report by clicking “Print”
6. Press “Ship” button - have Fed-EX shipping bill filled out
 - a. Enter FedEx shipment number

The screenshot shows a web application interface. At the top, there is a table with two empty columns. Below it, an 'Explorer User Prompt' dialog box is open, containing a text input field with the value '123456789987654321|' and 'OK' and 'Cancel' buttons. Below the dialog is a table with the following data:

	Sample ID	Collected On	Site Label	Subject Label	Sample Label
<input type="checkbox"/>	18908	09/03/2004	T	T1128	Aliquot - 1
<input type="checkbox"/>	18909	09/03/2004	T	T1128	Aliquot - 2
<input type="checkbox"/>	18913	09/03/2004	T	T1129	Aliquot - 1
<input type="checkbox"/>	18914	09/03/2004	T	T1129	Aliquot - 2
<input type="checkbox"/>	18918	09/23/2004	T	T1130	Aliquot - 1
<input type="checkbox"/>	18919	09/23/2004	T	T1130	Aliquot - 2

Below the table are three buttons: 'Delete Selected Samples', 'Ship', and 'Print'.

7. Click “OK”. A confirmation screen will appear telling you that your samples’ status has been changed in the system from “collected” to “shipped”. An email will be sent to the DCC and the Repository that has a link to the shipping manifest and tracking number.

The screenshot shows a confirmation screen. At the top, there is a 'Site:' dropdown menu set to 'Test' and a 'Continue' button. Below this, the email addresses 'PEGHC@umich.edu, darms@umich.edu, jbonner@med.umich.edu' are listed. The main message reads 'Samples marked as Shipped!' followed by a link: '[Click Here To Return Home](#)'.

8. The samples that you removed from the manifest will return the next time the manifest is opened .

Specimen Handling

A2ALL

Repository Info

- **Rutgers Genetics Repository** – collect a whole blood sample from donors and recipients at enrollment. This blood has to be shipped at room temperature the same day it's drawn.
- **McKesson Biosample Repository** – send samples of serum and tissue from various timepoints in the protocol, or in an event-driven encounter.

Supplies

- **DCC provides:**
 - pre-printed bar-coded sample labels to each site on a regular basis.
 - 2 ml cryovials for serum aliquots.
- **Rutgers provides:**
 - phlebotomy blood collection tubes
 - shipping kit.
- **ThermoFisher (McKesson) provides:**
 - shipping kit (including dry ice containers).
- **Your site will provide SST tubes and needles for blood collection**

Rutgers Genetics Repository Information

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What Rutgers needs from you...

- Prior notification of all incoming whole blood samples
- Full blood tubes from Phlebotomists
- Blood tubes must be inverted 6 times to assure solution within tube properly mixes with blood
- Always keep blood at room temperature

DO NOT REFRIGERATE

- NEVER put blood into FedEx drop boxes
- If drawing blood on Friday, mark for Saturday delivery or if on Saturday mark for Monday delivery
- Samples can be received Monday through Saturday

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Whole Blood Collection Steps

- Label tubes provided in Rutgers shipping kit
- Collect blood specimens in the labeled tubes
- Fill out the appropriate portions of the Phlebotomy Collection Form
- Package the blood tubes in the safety mailer
- Place the collection form in the mailer box outside of the plastic bag

Collection Steps Cont...

- Use the provided FedEx shipping label
- “Diagnostic Specimen Packed in Compliance with IATA Packing Instruction 650”
- Call Federal Express, 1-800-GO-FEDEX (1-800-463-3339), and a courier will be dispatched to pick up the samples.

NEVER PUT BLOOD KITS INTO A FEDEX DROP BOX!

Labeling Blood Tubes

- Absolutely NO personal identifiers should be on tubes, i.e. S.S.N, names, D.O.B., etc.
- All tubes must have a Study ID# (NIDDK#) to be accepted
- The Study ID# must begin with the site number, a hyphen, then a unique sample number
- If labels are being used, apply lengthwise on tube over original Vacutainer label, do not wrap around
- Leave at least a ¼ inch window along axis of tube for Rutgers technicians to measure volume & see separation of layers
- For all tubes labels should not cover rubber top

Applying Labels to Adult Tubes

Correct



Incorrect



FROM (NIDDK SITE):

SHIPMENT TO INCLUDE BLOOD
SAMPLES FOR CELL LINES

YELLOW TOP TUBES: _____

NIDDK STAFF: PLACE TUBE LABEL HERE OR COMPLETE BY HAND

(VERIFY INFO AGAINST INFO ON BLOOD TUBES!!!)

SEX: M ___ F ___

AGE: _____

ALTERNATE ID#: _____

NIDDK-ID#: _____

TO BE COMPLETED AT COLLECTION SITE:

DATE BLOOD DRAWN: _____ - _____ - _____ TIME DRAWN: _____ (24 HOURS) DRAWN BY: _____

CONTACT THE RUTGERS CELL & DNA REPOSITORY TO CONVEY PACKAGE TRACKING NO./DATE OF SHIPMENT (SEE BELOW). IF BLOOD IS SHIPPED ON A FRIDAY FOR SATURDAY DELIVERY, NOTIFY RUTGERS AND CHECK FEDEX FORM FOR SATURDAY DELIVERY.

EMAILED/FAXED/

CALL IN BY: _____

(SEE RUTGERS FAX/PHONE #S ABOVE)

_____/_____/_____
DATE

_____/_____/_____
TIME A/M/P/M

PACKAGE TRACKING #: _____

(CHECK SATURDAY DELIVERY ON DELIVERY FORM IF APPLICABLE)

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Proper Packaging of Rutgers Samples

- Packaging instructions are enclosed in every kit
- Place tubes into Styrofoam mailer with labels that have the NIDDK ID# facing down
- Secure tubes in place with lab tape.

Correct



Incorrect



Key NIDDK Contact Personnel at Rutgers

- **Dana Witt** – Communications Director
witt@biology.rutgers.edu
- **Dale Hayward** – Communications Coordinator
heyward@biology.rutgers.edu Tel: (732) 445-1498
- Please note that you can use the following email address to reach all staff at the Rutgers office. You may place shipping kit orders through this email:
commstaff@biology.rutgers.edu
 - Kits come 25 to a case
 - Kits should be requested at least 4 weeks before current supply runs out in order to ensure timely delivery

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ThermoFisher Biosample Repository (McKesson)

- All samples, except for Rutgers whole blood specimens, are shipped to ThermoFisher (McKesson)
 - Serum aliquots (Frozen)
 - Liver Tissue (Ambient & Frozen)
- Shipping Kits are provided by the Repository.

Aliquot Samples

- Aliquot serum from SST into cryovials
- 4.0ml of serum should be available to be divided into ten 400 µl aliquots
- If there is less volume, fill as many vials with 400 µl as possible
- Do NOT divide equally into the vials
- ****Barcode Scan in BioDBx****
- Place **labeled** cryovials with aliquots in -70°C freezer
- Stored samples will be batch-shipped to McKesson each month (**see schedule**)

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Collecting Liver Tissue

- Local arrangements for specimen collection from the OR will apply.
- Each biopsy is cut into thirds; 2 in RNALater (then frozen), 1 in paraffin block (ambient)
- The presence of a study coordinator in the OR may expedite both the labeling of the specimen and its prompt handling

Shipping Samples to the Biosample Repository

Shipping Schedule

- Chicago/New York - First Monday of each month
- Colorado/Penn – Second Monday of each month
- Virginias/UNC – Third Monday of each month
- UCLA/UCSF – Fourth Monday of each month



Sample Shipping (cont'd)

- **Print a manifest from BioDBx**
- **Use the appropriate kit (ambient or frozen)**
- **Pack the specimens according to the instructions included with the shipping kit**
- **Enter the weight of the dry ice as 4kg**
- **Put the appropriate stickers on the box**
- **Use the pre-printed FedEx airbill.**
- **Call Federal Express (1-800-GO-FEDEX) and FedEx will dispatch a courier to pick up the package**

NIDDK Biosample Repository Shipping Address

**Fisher BioServices
20301 Century Blvd.
Bldg. 6, Suite 400
Germantown, MD 20874**

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NIDDK Biosample Repository Supply Orders

**Please use our group email address to
order supplies and send shipment
notifications:**

Bio-NIDDKRepository@thermofisher.com

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Other Contact Information

Heather Higgins

Principal Investigator

Office: 240-686-4703

Heather.Higgins@thermofisher.com

Sandra Ke

Assistant Principal Investigator

Office: 240-686-4702

Sandra.Ke@thermofisher.com

Clifford Snell

Contract Administrator

Office: 240-686-4706

Clifford.Snell@thermofisher.com

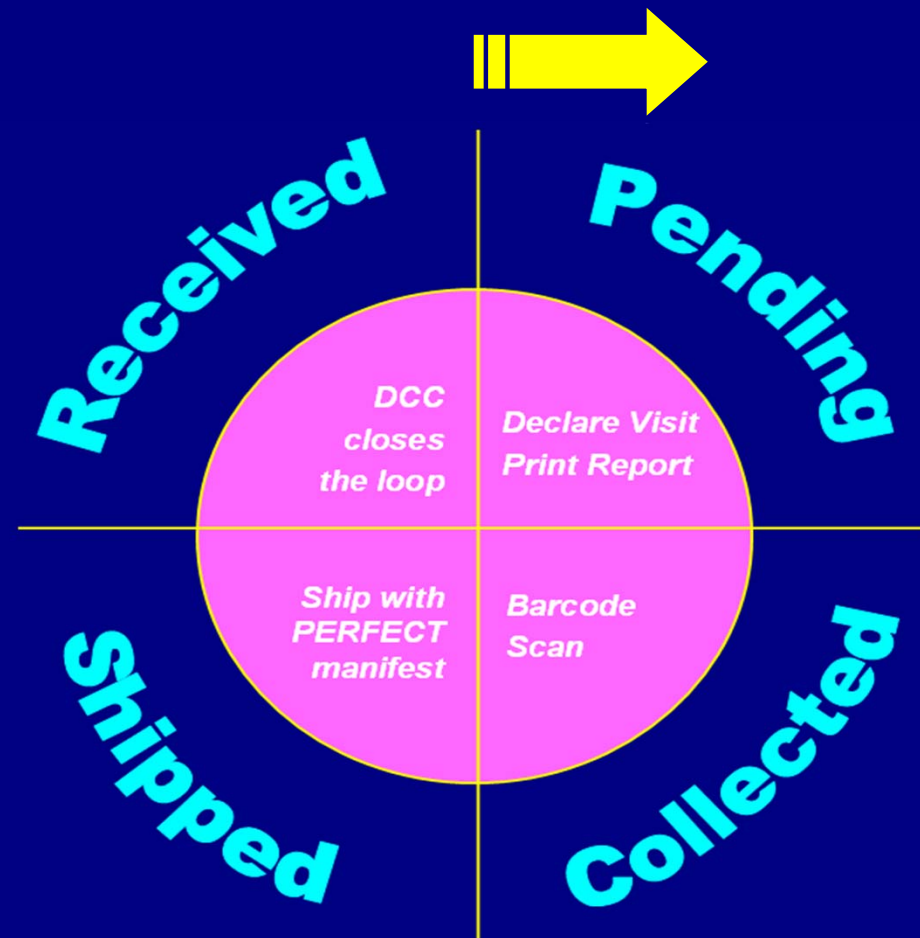
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Sample Handling in BioDBx

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Cohort Study Sample Handling Process

The Cycle



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Cohort Study Sample Handling Process

The Cycle



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BioDBx Labels

- Labels are printed by the DCC and sent out to the sites via FedEx.
- When enrolling a subject, BioDBx will assign the next available subject number to your new enrollee, and the labels for this subject should already be at your site.
- When you are ready to collect a sample, you will go into BioDBx and associate the pre-printed labels with the subject, visit type and sample type.

Time points for which there are no labels

- Pre-printed labels only go up to Year 5 (Month 60)
- Some subjects (Cohort Lite, Former Retro, etc.) will have follow-up beyond these time points.
 - For these subjects, unused labels can be used for later time points.

Label Change Procedures

- Declare visit on PHI page
- Write correct time point on label
- Email Abby (abbysmit@umich.edu) with the following information:
 - Subject ID #
 - Original time point from label
 - Actual time point from sample
 - Sample type (serum vs. bx)
 - Sample numbers

Cohort Study Sample Handling Process

The Cycle



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Logging Samples in BioDBx

- Scanning labels
- Scanning printed barcode report

A note about the importance of logging samples

- **If you do not log samples they will not move to the next stage of the cycle and you will not receive credit for having collected them.**
- **The Steering Committee regularly reviews sample handling status, so it is important that the status of you samples remains up to date to insure accurate reporting.**

Cohort Study Sample Handling Process

The Cycle



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Electronic Shipping

- **Preparing your manifest**
 - Make sure your manifest matches what's in your box.
 - * *Note: If you back out of your manifest all deleted samples will return.*
 - Have your FedEx tracking number on hand before preparing your manifest.
- **Pressing the “Ship” button**
 - This is the point of no return so make sure your manifest is correct.
 - BioDBx will automatically generate an email to the repository, the DCC, and the shipper, that the samples have been sent.

Things to Know about Shipping

- **Unlogged samples will not show up on your manifest.**
- **When they receive samples, the repository checks the manifest against the box. Any discrepancies must be reconciled.**
- **The database can only handle so many samples per manifest. If you have too many samples built up on your manifest, you will not be able to open it. Please ship regularly to avoid this problem.**

Your Responsibilities in Accurate Sample Handling

- Declaring visits
- Logging samples
- Accurate electronic shipping
- Shipping regularly
- Informing the DCC of label changes

Cohort Study Sample Handling Process

The Cycle



When to Call the DCC

Please feel free to call us whenever you have any questions about BioDBx and sample handling.

Abby and Monique
(734) 998 6580

abbysmit@umich.edu

mlowe@umich.edu

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Recipients:

Time Point	Forms	Samples/Procedures	Comments
Enrollment	<ul style="list-style-type: none"> RCP Demographics RCP Condition @ Enrollment QOL Assessment (SF-36) HCC @ Enrollment HCV @ Enrollment 	<ul style="list-style-type: none"> 3 ACD tubes whole blood-Rutgers HLA Typing 15 ml of blood for Biosample Repository serum (two 7.5ml SST tubes) Blood for labs Imaging for HCC HCV labs 	24 ml whole blood (Genetics Repository)
Pre-TXP Quarterly Assessment 1-5	<ul style="list-style-type: none"> RCP Pre-TXP Quarterly Assessment 1-5 QOL Assessment (SF-36) HCC Pre-TXP Quarterly Assessment 1-5 HCV Pre-TXP Quarterly Assessment 1-5 RCP Hospitalizations 	<ul style="list-style-type: none"> 15 ml of blood for Biosample Repository serum(two 7.5ml SST tubes) Blood for labs Imaging for HCC Labs for HCV 	10 serum aliquots 0.4ml each (Biosample Repository) Each hospitalization requires a separate form.
Transplant	<ul style="list-style-type: none"> RCP Condition @ TXP RCP Intraop HCC @ TXP HCC Explant Assessment HCV @ TXP RCP Hospitalizations AE/SAE Form 	<ul style="list-style-type: none"> 1 Tru-cut Bx-back table, cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) 1 Tru-cut Bx 30-60 minutes post-reperfusion cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) 	The TXP counts as a hospitalization and may be completed at discharge visit Each blood draw = 10 serum aliquots 0.4ml each (Biosample Repository)

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

		<ul style="list-style-type: none"> • 15 ml blood (two 7.5ml SST tubes) for Biosample Repository serum at pre-op • Blood for TXP day preop labs • 15 ml blood (two 7.5ml SST tubes) for Biosample Repository serum at the same time points of the Bx's (anhepatic & 30-60 minutes post-reperfusion) • HepB and HCV status of donor for DDLT recipients • HCV labs 	
Day 1 post-txp	None	<ul style="list-style-type: none"> • 15 ml blood (two 7.5ml SST tubes) for Biosample Repository serum 	10 serum aliquots 0.4ml each (Biosample Repository)

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Recipients:

Time Point	Forms	Samples/Procedures	Comments
Week 1 Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 1 Week Post-TXP RCP Morbidity RCP Hospitalizations Rejection Episodes AE/SAE Form HCV @ 1 Week Post-TXP 	<ul style="list-style-type: none"> 15 ml blood for Biosample Repository serum. Blood for labs *1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Paraffin Block for Biosample Repository) HCV labs 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>*Bx only if rejection episode</p> <p>Each hospitalization, morbidity and rejection episode requires own form</p>
2 Weeks Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 2 Weeks Post-TXP RCP Morbidity RCP Hospitalizations Rejection Episodes AE/SAE Form 	<ul style="list-style-type: none"> 15 ml blood for Biosample Repository serum. Blood for labs *1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Paraffin Block for Biosample Repository) 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>*Bx only if rejection episode</p> <p>Each hospitalization, morbidity and rejection episode requires own form</p>
1 Month post TXP	<ul style="list-style-type: none"> RCP Condition @ 1 Month Post-TXP HCV @ 1 Month Post-TXP HCV Biopsy Pathology Report RCP Morbidity 	<ul style="list-style-type: none"> 15 ml blood for Biosample Repository serum. Blood for labs HCV labs 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>*Bx only if treated HCV recurrence</p>

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

	<ul style="list-style-type: none"> • RCP Hospitalizations • Rejection Episodes • AE/SAE Form 	<ul style="list-style-type: none"> • *1 Tru-cut Bx prior to treatment of HCV recurrence; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) • **1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) 	<p>**Bx only if rej. episode Each hospitalization, morbidity and rejection episode requires own form</p>
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Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Recipients:

Time Point	Forms	Samples/Procedures	Comments
3 Months Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 3 Months Post-TXP QOL Assessment (SF-36) HCV @ 3 Months Post-TXP HCV Bx Pathology Report RCP Morbidity RCP Hospitalizations Rejection Episodes AE/SAE Form & Tracking Form 	<ul style="list-style-type: none"> 15 ml blood for Biosample Repository serum. Blood for labs, AFP Protocol Bx for HCV patients: 1 Tru-cut Bx cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) *Bx: 1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) MRI/CT to measure liver volume for Regeneration study (day 91) Prednisone dose in mg. 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>*Bx only if rejection episode or treated HCV recurrence</p> <p>Each hospitalization, morbidity and rejection episode requires its own form</p>
6 Months Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 6 Months Post-TXP QOL Assessment (SF-36) RCP Morbidity HCV Bx Pathology Report HCC @ 6 Months Post-TXP RCP Hospitalizations Rejection Episodes 	<ul style="list-style-type: none"> 15 ml blood for Biosample Repository serum. Blood for labs, AFP HCC Imaging *Bx: 1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>*Bx only if rejection episode</p> <p>Each hospitalization, morbidity and rejection episode requires own form</p>

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

	<ul style="list-style-type: none"> • AE/SAE Form 	<p>be made into Parafiin Block for Biosample Repository)</p> <ul style="list-style-type: none"> • **1 Tru-cut Bx prior to treatment of HCV recurrence; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) 	<p>**Bx only if treated HCV recurrence</p>
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Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Recipients:

Time Point	Forms	Samples/Procedures	Comments
1 Year Post-TXP	<ul style="list-style-type: none"> RCP Condition @ 1 Year Post-TXP QOL Assessment (SF-36) HCC @ 1 Year Post-TXP HCV @ 1 Year Post-TXP HCV Bx Pathology Report RCP Morbidity RCP Hospitalizations Rejection Episodes AE/SAE Form 	<ul style="list-style-type: none"> 15 ml blood for Biosample Repository serum. Blood for labs, AFP Protocol Bx for HCV patients: 1 Tru-cut Bx cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) HCC Imaging HCV labs *1 Tru-cut Bx prior to treatment of HCV recurrence; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) **1 Tru-cut Bx prior to treatment of rejection episode; cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Parafiin Block for Biosample Repository) 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>Each hospitalization, morbidity and rejection episode requires its own form</p> <p>*Bx only if treated HCV recurrence</p> <p>**Bx only if rejection episode</p>
18 Mos Post-TXP	<ul style="list-style-type: none"> HCC @ 18 Months Post-TXP 	<ul style="list-style-type: none"> AFP 	HCC patients only
2 Years Post-TXP	<ul style="list-style-type: none"> Same as 1 Year Post-TXP 	<ul style="list-style-type: none"> Same as 1 Year Post-TXP 	Same as 1 Yr Post-TXP
3 Years Post-TXP	<ul style="list-style-type: none"> Same as 1 Year Post-TXP 	<ul style="list-style-type: none"> Same as 1 Year Post-TXP 	Same as 1 Yr Post-TXP

Required @ This Time Point
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Cohort Study Time Points and Corresponding Forms and Samples

		except no HCC imaging	
4 Years Post-TXP	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP 	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP except no HCC imaging and no HCV Protocol Bx 	Same as 1 Yr Post-TXP
5 Years Post-TXP	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP 	<ul style="list-style-type: none"> • Same as 1 Year Post-TXP except no HCC imaging and no HCV Protocol Bx 	Same as 1 Yr Post-TXP

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Donors:

Time Point	Forms	Samples	Comments
Enrollment/Donor Evaluation	<ul style="list-style-type: none"> • Donor Demographics • Donor Evaluation • Full QOL and Motivation 	<ul style="list-style-type: none"> • 3 ACD tubes of whole blood to Rutgers Genetics repository • 15 ml blood draw for Biosample Repository serum. • Blood for labs • Homocysteine level 	<p>24 ml whole blood</p> <p>10 serum aliquots 0.4ml each (Biosample Repository)</p>
At Donation	<ul style="list-style-type: none"> • Donor Intraop • Donor Hospitalizations 	<ul style="list-style-type: none"> • HLA Typing • 1 Tru-cut Bx prior to removal, cut into thirds; 2 in RNALater, 1 in formalin (to be sent to Path to be made into Paraffin Block for Biosample Repository) • 15 ml blood for Biosample Repository serum. • Blood for labs pre-op • 15 ml blood for Biosample Repository serum at the same time as the Bx • 15 ml blood for Biosample Repository serum 30-60 min. after crossclamp 	<p>The donation surgery counts as a hospitalization and form may be completed at discharge visit</p> <p>Each blood draw = 10 serum aliquots 0.4ml each (Biosample Repository)</p>
Day 1 post-txp	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • 15 ml blood for Biosample Repository serum. • Blood for labs 	
1 Week Post-	<ul style="list-style-type: none"> • Donor Condition @ 1 Week Post-Donation 	<ul style="list-style-type: none"> • 15 ml blood for Biosample 	10 serum aliquots 0.4ml each

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Donation	<ul style="list-style-type: none"> • Donor Hospitalizations • Donor Morbidity/Complications • AE/SAE Form 	<ul style="list-style-type: none"> Repository serum. • Blood for labs 	<p>(Biosample Repository)</p> <p>Each hospitalization and morbidity requires a separate form</p>
1 Month Post-Donation	<ul style="list-style-type: none"> • Donor Condition @ 1 Mon. Post-Donation • Donor Hospitalizations • Donor Morbidity/Complications • AE/SAE Form 	<ul style="list-style-type: none"> • 15 ml blood for Biosample Repository serum. • Blood for labs 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>Each hospitalization and morbidity requires a separate form</p>

Required @ This Time Point
Diagnosis-Linked
Event-Linked



Cohort Study Time Points and Corresponding Forms and Samples

Donors:

Time Point	Forms	Samples/Procedures	Comments
3 Months Post-Donation	<ul style="list-style-type: none"> • Donor Condition @ 3 Mos Post-Donation • Full QOL and Motivation • Donor Hospitalizations • Donor Morbidity/Complications • AE/SAE Form 	<ul style="list-style-type: none"> • 15 ml blood for Biosample Repository serum. Blood for labs • MRI/CT for Regeneration study (day 91) 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>Each hospitalization and morbidity requires a separate form</p>
1 Year Post-Donation	<ul style="list-style-type: none"> • Donor Condition @ 1 Year Post-Donation • Full QOL and Motivation • Donor Hospitalizations • Donor Morbidity/Complications • AE/SAE Form 	<ul style="list-style-type: none"> • 15 ml blood for Biosample Repository serum. Blood for labs 	<p>10 serum aliquots 0.4ml each (Biosample Repository)</p> <p>Each hospitalization and morbidity requires a separate form</p>
2 Yrs Post-Donation	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	Same as 1 Yr Post Donation
3 Yrs Post-Donation	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	Same as 1 Yr Post Donation
4 Yrs Post-Donation	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	Same as 1 Yr Post Donation
5 Yrs Post-Donation	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	<ul style="list-style-type: none"> • Same as 1 Year Post-Donation 	Same as 1 Yr Post Donation

A2ALL REPOSITORY GUIDELINES

SERUM and TISSUE SAMPLE PREPARATION

Feb. 2, 2005

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1. Center numbers for the Repository

Each site has been assigned a center number that must be used when shipping samples to the repository. A2ALL sites are identified uniquely by a two digit number listed in the table below:

PI	Site	Site	NIDDK Site Number
Emond	New York	Columbia Presbyterian	310
Abecassis	Chicago	Northwestern University	311
Shaked	Philadelphia	University of Pennsylvania Health System	312
Trotter	Denver	University of Colorado Health System	313
Ghobrial	Los Angeles	University of California, Los Angeles	314
Freise	San Francisco	University of California, San Francisco	315
Fair	Chapel Hill	University of North Carolina	316
Berg	Charlottesville	University of Virginia Health System	317
Fisher	Richmond	Virginia Commonwealth University	318

2. Specimen Repositories

There are two repositories:

1. NIDDK has contracted with the Rutgers University Cell & DNA Repository (Genetics Repository) to establish cell lines or to extract PBMC's and DNA from whole blood. Whole blood for cell lines, or for DNA and PBMC extraction, will be shipped immediately upon collection to the repository at Rutgers.
2. NIDDK has established a Biosample Repository (McKesson) for long-term storage of blood, tissue specimens and slides (i.e., all samples except the whole blood that is sent to Rutgers University). Samples will be processed as described below, frozen and then shipped via licensed overnight carrier once every month to the NIDDK repository.

All specimens will be labeled with a research study subject identifier and a vial barcode that will include the site number, but will be otherwise de-identified prior to shipment to either location. All samples will be accompanied by a shipping manifest that will describe the content of each vial. Receipt of samples by the repository will be acknowledged to the originating center.

3. Schedule for Specimen Collection

3.1. From the Recipient

Blood and samples from the recipient will be collected at:

Time of initial evaluation/enrollment

Quarterly visits pre-transplant (starting from enrollment)

Transplantation (2 samples)

Day one post-transplant

1 week post-transplant

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2 week post-transplant

1 month post-transplant

3 month post-transplant

6 month post-transplant

12 month post-transplant

Annually thereafter until study ends

Blood samples should be drawn at the same time as blood is taken for clinical testing or when there is IV access for a clinical procedure.

At each of the above times, draw:

- 15 ml of whole blood in SST vials for serum

At the enrollment visit ONLY, also draw:

- 24 ml of whole blood in three 8 ml ACD vials provided by the Rutgers University Cell & DNA Repository.

Other Specimens: At transplantation tissue samples will be collected on all recipients and liver samples will be collected from HCV positive recipients at selected visits. See section 5.4 for a description of these samples.

3.2. From the Donor

Blood and samples from the donor will be collected at:

Time of initial evaluation/enrollment

Donation surgery (3 samples)

Day one post-transplant

1 week post-transplant

1 month post-transplant

3 month post-transplant

12 month post-transplant

Annually thereafter until study ends

Blood samples from each donor will be obtained, when possible, at the time of consent or at a convenient time during the ongoing clinical evaluation. From each donor, at each visit listed above, draw:

- 15 ml of whole blood in an SST vial for serum

At the transplant visit ONLY, also draw:

- 24 ml of whole blood in three 8 ml ACD vials provided by the Rutgers University Cell & DNA Repository.

Other Specimens: At donation, tissue samples will be collected from all donors. See section 5.4 for a description of these samples.

The processing of the blood samples from the donors is the same as that for the recipient

4. Rutgers University Cell & DNA Repository (RUCDR)

The RUCDR will provide all the supplies (except labels for the vacutainers) that the site needs to collect and ship whole blood to the RUCDR. The RUCDR will ship to each site cartons containing 25 kits.

Each kit will contain a set of three 8.5 ml ACD vacutainer vials. The whole blood must be shipped on the day of collection to the RUCDR.

Each kit consists of:

- a cardboard box that should be used to ship the samples,
- a Styrofoam box containing the vacutainers and packing material
- red, water-proof tape
- a press-lock plastic bag
- instructions
- phlebotomy collection form
- FEDex Airbill

Follow the instructions that are provided. They describe how to:

- Label the vacutainers.
- Collect the sample in the vacutainers that are provided.
- Shake the vacutainers.
- Pack the vacutainers in the boxes.
- Complete the phlebotomy collection form
- Complete the Airbill – note that there is already an account number on it and.
- Call FEDex so the package is picked up that day – do NOT keep the sample overnight.

The RUCDR Phlebotomy Collection Form refers to a NIDDK-ID# and an alternate ID#. The **NIDDK-ID#** is the three digit NIDDK site ID followed by a hyphen followed by the assigned BioDBx sample number.

The **alternate ID number** is a second identifier in case the first is unreadable and this will be the subject ID number. You will need to copy the numbers onto the RUCDR Phlebotomy Collection Form.

4.1. Whole blood for the Rutgers University Cell & DNA Repository

Preparation for immortalized cell lines or DNA extraction

Be sure the following materials are readily accessible in addition to what is needed for plasma handling.

- Recipient or Donor: Three 8.5 ml ACD vials provided by the Rutgers University Cell & DNA Repository.

4.2. Specimen handling for the Rutgers University Cell & DNA Repository

- The Rutgers University Cell & DNA Repository will supply all the blood vacutainer tubes and packaging material to be used.
- **DO NOT write the patient's name or any other personal identification information (e.g. SS#, DOB) on the tubes.**
- Affix the appropriate subject's bar code label onto each vial-note that the three RUTGERS blood collection tubes will all have the same label attached for each patient (same sample number assigned)
- Complete the Phlebotomy Collection Form: The top panel is completed by the RUCDR. The RUCDR Phlebotomy Collection Form refers to a NIDDK-ID# and an alternate ID#. The NIDDK-ID# is the three digit site ID followed by a hyphen followed by the assigned BioDBx sample number. The alternate ID number will be the subject ID number. You will need to copy the numbers onto the RUCDR Phlebotomy Collection Form.
- Collect blood specimen into the three vacutainer tubes.
- After collecting whole blood into the tubes, gently invert the tube 6 times to mix with additives and keep them at room temperature.
- Double check subject ID, verify that ID information on tube matches that on the enclosed NIDDK Phlebotomy Collection Form.
- Date and sign the NIDDK Phlebotomy Collection Form – TO BE COMPLETED IN PHLEBOTOMIST area. *Make two copies of this form – one to be kept in the research file and the second to be sent to the Repository.*
- Package the blood tubes in the safety mailer following the enclosed instructions. Be sure to seal the Styrofoam container with the red water resistant tape.
- Place the NIDDK Phlebotomy Collection Form in the mailer box outside of the plastic bag. Tape the cardboard box closed when the assembly is complete.
- Use the enclosed Fed Ex shipping label to ship the sample to the Rutgers University Cell & DNA Repository. Be sure the shipping label is marked for priority overnight delivery.
- For routine shipments, be sure the outside of the box is labeled "Diagnostic Specimen Packed in Compliance with IATA Packing Instruction 650."
- Update BioDBx with date of sample and bar code labels used-Status = shipped
- **Call Federal Express, 1-800-GO-FEDEX (1-800-463-3339)**, and a courier will be dispatched to pick up the samples.
- **Notify Emily Gymnich and Jacqueline Sabb at the Rutgers University Cell and DNA Repository** that blood is being shipped and provide the Federal Express tracking number(s) _____ and NIDDK ID #(s) _____. This can be done by email (gymnich@biology.rutgers.edu and sabb@biology.rutgers.edu), fax (1-732-445-1149), or phone (1-732-445-1498). **THIS WILL BE DONE AUTOMATICALLY BY BioDBx**

Address: Dr. Douglas Fugman/Genetics

Rutgers Univ. Cell & DNA Repository
Div. Life Sciences-Nelson Labs
604 Allison Road (Rm C120A)

5. NIDDK Biosample Repository (McKesson) and Sample Handling

All samples, except the whole blood for cell lines or DNA, are shipped to the NIDDK Biosample Repository. All shipping materials will be provided by the repository. This includes:

Each shipping kit consists of:

- a cardboard box that should be used to ship the samples,
- a large Styrofoam box
- 3 81-well cardboard vial boxes
- instructions for shipping
- FEDEX Airbill

The DCC will provide each site with:

- 2 ml cryovials for the aliquots
- bar coded shipping labels for the vials (one set for each patient)

5.1. Serum for the NIDDK Biosample Repository

Preparation for Serum Collection

Be sure the following materials are readily accessible before performing venipuncture: All necessary tubes, identified for size, draw, and additive; labels for the tubes.

Recipients and Donors:

- Two 7.5 ml SST tube
- 10 storage cryovials, labeled in advance with supplied patient specific labels-use correct visit and sample type labels

Serum specimen handling:

- Blood will be drawn using two 7.5 ml serum separator tubes (SST) according to each hospital's venipuncture procedure.
- After collection of whole blood into the SST tube, gently invert the tube 8-10 times.
- After mixing, store the SST tube upright at room temperature until centrifugation.
- Blood samples should be centrifuged **within 2 hours** for best results.
- Centrifuge SST tube/blood sample at room temperature (18-25°C) in a horizontal rotor (swing-out head) for a minimum of 10 minutes at 1,100 RCF (Relative Centifugal Force).
- Be sure that there is not any subject identifying material on the cryovials that will be sent to the repository.

Use the 10 labeled cryovials

- Aliquot serum into cryovials

4.0 ml of serum should be available to be divided into ten 400 µl aliquots

If there is less volume, fill as many vials with

400 µl as possible – **do NOT divide equally into the vials**

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- Enter BioDBx and associate the patient specific barcode labels with the sample dates
- Place cryovials with aliquots in -70°C freezer
- Stored samples should be batch shipped every month

5.2. Tissues obtained at surgery or at time of biopsy

Preparation for tissue specimens

For each type of specimen described below, prepare (2 ml vial) vials with patient specific labels:

Tru-Cut needle biopsy tissue core should be divided into three equal pieces.

Have three labeled 2ml cryovials ready-two filled with 1 ml of RNALater and one filled with 1 ml of formalin. Make sure the liquid is not close to the top of vial due to expansion. After the vial is capped and tissue has been placed inside-invert several times to ensure that tissue is completely submerged. Store the vial in upright position.

- Label the 2 ml cryovials with the repository bar codes and remove any institutional identifiers prior to the following procedure.
- Add either formalin or RNALater to the cryovials (be sure to leave room at the top to allow for freezing expansion)
- Place the liver tissue into cryovial.
- Keep Formalin vials at ROOM TEMPERATURE-do not refrigerate or freeze
- Place RNALater vials into -70°C freezer immediately (may be stored in a refrigerator for up to 5 days if freezer access is delayed) until shipment to central repository.
- Update BioDBx with dates of each sample obtained and bar code labels used.
- Frozen liver tissue can be sent with batch shipments of serum. Liver tissue in Formalin must be sent separately at room temperature-DO NOT send with frozen tissue/serum samples.

Transplantation: There are three intraoperative biopsy samples for LDLT and only two (steps #2 and #3) for DDLT

- 1) Donation surgery obtain Tru-Cut needle liver biopsy of right segment along line of resection prior to parenchymal dissection
- 2) Back table: obtain Tru-Cut needle biopsy of donated segment
- 3) 30-60 minutes post-reperfusion: obtain Tru-Cut needle biopsy

Post-transplantation: For HCV positive recipients at the time of protocol biopsies-a percutaneous biopsy tissue core should be obtained. Protocol biopsies are scheduled post-transplant months 3, 12, 24 and 36. Each core should be divided into three equal pieces and packaged as above.

During a liver biopsy for rejection, extra biopsy material will be collected when possible. Based on availability after samples needed for clinical diagnosis, a Tru-Cut needle sample may be obtained and divided into three equal pieces and stored as noted above.

6. Specimen handling

Local arrangements for the specimen collection from the operating rooms will apply. It is essential that the specimens are handled immediately—FASTER is better. The presence of a study coordinator in the operating room at the time of transplant surgery may expedite both the labeling of the specimen.

- All labels are provided by the DCC for each study subject. Keep the individual subject labels separate.
- Specimens are to be inserted in labeled vials.
- Please use the label that is appropriate for the sample.
- Wrap the label lengthwise along the vial.
- Remove all other subject identifiers from the vial.
- Update BioDBx as soon as samples are obtained with date of sample.
- All specimens should be sent to the repository with the monthly shipment.

7. Labels Provided for each subject

Whole blood for **Rutgers** repository (enrollment only)

Serum from the recipient

Serum from donor

Liver Biopsy Tissue Core Samples

7.1 Completing the Shipping Manifest Form

Fill in the header information on the form: (Some of the header information may be preprinted on the form).

- Site and Subject ID: The site id is the three digit number assigned on page 2 above (e.g. Columbia 310). The subject ID is the BioDBx subject number
- Initials of the research staff member who is sending the form and specimen to the repository. Use initials as they appear on the site signature log.
- Date that the sample was collected from the subject (not the date of shipping)
- Date of shipment. Date shipped to repository
- FedEx tracking number from the FedEx airbill.

7.2 BioDBx Sample Tracking – Detailed information

Cohort Study BioDBx Sample Handling Documentation

1. Preparation for subject visit
 - a. Locate the pre-printed labels that the DCC sent to your site. Choose the batch of labels that correspond to the subject's BioDBx number. Put those labels in a location where you can access them for the rest of the study.
 - b. Once you know the date the next visit is scheduled, declare the visit for subject. **YOU MUST DECLARE THE VISIT OR NONE OF THE SUBJECT AND SAMPLE REPORTS WILL WORK PROPERLY!**

- i. Scroll down on the PHI page to the “Contact” window.

Enroll New Subject
Show All Subjects
Search for Subject

Current User: Joe Bonner [Logout]
 Current Study: A2COH
 Current Site: Test
 Study Programs:
[Demo Web Pages](#)

Contact No.	Contact Date	Contact Type	Made By	Comment	Samples	Actions
	10/15/2004	Enrollment	JBONNER		To Samples	Update/Remove Enter Data
		Qtr1			To Samples	Update/Remove Enter Data
		Qtr2			To Samples	Update/Remove Enter Data
		Qtr3			To Samples	Update/Remove Enter Data
		Qtr4			To Samples	Update/Remove Enter Data
		Qtr5			To Samples	Update/Remove Enter Data
		Txp/Dntn Surg			To Samples	Update/Remove Enter Data
		Day 1			To Samples	Update/Remove Enter Data
		Week 1			To Samples	Update/Remove Enter Data

- ii. Find the appropriate contact timepoint and click “Update/Remove”. A dialogue box will pop up enter the date and “contact made by” fields. If you have any comments you’d like to make, enter them in the box.

Update/Remove Contact for A2COH-R1012

Contact Type Enrollment

Contact Made By

Contact Date *
(format: mm/dd/yyyy)

Comment

Remove

Update/Remove Contact
Cancel the Changes
Close

Note: * fields value required.

- iii. Click the “Update/Remove Contact” Button. Your new contact will be updated and the screen will go back to the PHI/Study Enrollment page.
- iv. Repeat the above steps for each patient visit that is scheduled.

- c. You can now choose to enter data for this subject by clicking the “Enter Data” button.
- d. To update other future contacts, you can access the “Update/Remove Contact” menu by searching for the subject and clicking on the “PHI” button.

2. Printing Bar Codes on Paper

- a. Install the font that the DCC sent you.

- i. Drag it from your email to your desktop and open up your Control Panel.
 - ii. Click on Fonts.
 - iii. In the file menu, click on "Install New Font", and point the destination at your desktop where the font is located.
 - iv. Alternatively, you can copy the font to your clipboard by highlighting it, holding your "Control" Key and the "C" key down at the same time.
 - v. Open your Control Panel and Font folder and hold your "Control" key and the "V" key down at the same time. This will paste the font into the proper folder. You may need to ask your IT staff for help if you don't have install privileges on your computer.
- b. You may print an 8.5" X 11" page of bar codes that correspond to the labels for all of the subjects for whom you've declared a visit. These are for use when scanning the actual samples' bar codes into the system isn't convenient or feasible (i.e. the samples are in the clinic area and you are updating sample collection at your computer in your office).
- c. In BioDBx, click on the Sample Tracker program in the Study Programs window on the upper right side of your screen.



- d. Choose your site.
- e. Click on the folder that says "This Week"
- f. Click on Pending Samples
- g. Scroll Down
- h. Click on Print This Report
- i. Note that the report is by Site. So, you will be viewing all samples that you are expecting to collect from visits you have declared. This may involve multiple subjects and time points.
- j. You can use this reporting feature to look at what samples you have collected and shipped during a current or past week.
- k. You can also see what samples have been received by choosing that report. There will be a delay in seeing what is received since the repository only reports this information to the DCC every two weeks.

Please Choose a site

- Sample Processing Report for A2COH (T) 02-Feb-2005 15:46:08
 - This Week (30-Jan-2005 - 05-Feb-2005)
 - Samples: COLLECTED
 - Samples: PENDING
 - Samples: RECEIVED
 - Samples: SHIPPED
 - Past Weeks
 - Future Weeks

A2COH Sample Processing Report for Northwestern 02

Samples: PENDING for the week beginning 30-Jan-2005

Report run on 02-Feb-2005 15:46:35

Subject	Sample	Status	Type	Date	Contact
R1106	PENDING	Serum Aliquot	Enrollment	->	McKesson



3. Collecting Samples

- Collect the appropriate samples from the patient for that time point, and if necessary, aliquot and place in the appropriate labeled storage vials.
- There is a unique value for each planned sample that goes to McKesson. The 3 tubes of blood for the Genetics Repository all have the same Sample ID.
- Click the link to the Sample Processor in the Study Programs area of BioDBx:

Current User: Joe Bonner [\[Logout\]](#)
Current Study: A2COH
Current Site:
Study Programs:
Demo Web Pages:

In the "Action" box, choose "Log Samples", then click the "Continue" button

Site: Test <input type="button" value="Continue"/>	Action: Log Samples <input type="button" value="Continue"/>	
--	---	--

- d. Scan the bar code for the first sample. Hit the "Tab" key
- e. The fields (other than the date) will prepopulate. Click the "Insert" button. On the lower left, you will see a "Success" message that tells you that you have successfully entered that sample. If you are scanning samples the same day they are drawn then you can leave the date blank today's date will be automatically entered. If you are scanning a date in the past then enter that date information in the "Collected On" box.

Site: Test <input type="button" value="Continue"/>	Action: Log Samples <input type="button" value="Continue"/>	
--	---	--

Sample ID	Collected On	Site Label	Subject Label	Sample Label	
18918	09/23/2004	T	T1130	Aliquot - 1	Seru
18919	09/23/2004	T	T1130	Aliquot - 2	Seru
18916	09/23/2004	T	T1130		Who

Success

- f. Continue scanning and entering samples (for all patients) until you have entered all of the samples you have collected. When you are done inserting the last sample (make sure you click "Insert" for that last sample), Click the "Log Samples" button. You will see a confirmation screen telling you that the samples' status has changed from "Pending" to "Collected"

Site: Test <input type="button" value="Continue"/>	Action: Log Samples <input type="button" value="Continue"/>	
--	---	--

Your Samples have been added to the Log and their status has been updated to Collected

[Click Here To Return Home](#)

- g. The sample's status will change in the subject's information panel as well. You can confirm this by searching for the subject and clicking the blue "samples" button.

Enroll New Subject Show All Subjects Search for Subject

Current User: Steve Middlekauff [Logout]
 Current Study: A2COH
 Current Site: Test
 Demo Web Pages

Current Subject: T1136

[View Subject Samples](#) | [Update Samples](#) | [Add Samples](#) | [Samples Report](#) | [Mole Query](#) | [To Lots](#) | [Storage Units](#)

Brief View Lists View Lots & Lists View

Sample Type	Date Received	Sample Label	Sample Status	Quantity	
Serum (18948)		Aliquot - 1	COLLECTED	1	Sample Record Print Barcode Child Samples (0)
Serum (18949)		Aliquot - 2	COLLECTED	1	Sample Record Print Barcode Child Samples (0)
Whole Blood (18946)			COLLECTED	2	Sample Record Print Barcode Child Samples (0)

4. Preparing samples for shipment

- a. Click the link to the Sample Processor in the Study Programs area of BioDBx:

Enroll New Subject Show All Subjects Search for Subject

Current User: Joe Bonner [Logout]
 Current Study: A2COH
 Current Site: Test
 Study Programs: [Sample Processor](#)
 Demo Web Pages

- b. Choose "Prepare Shipment" action. Click "Continue"

Site: Test Continue	Action: Prepare Shipment Continue	
------------------------	--------------------------------------	--

- c. Choose To Rutgers or To McKesson or To McKesson Cold. Click "Continue"

Site: Test Continue	Action: Prepare Shipment Continue	Select Action: To McKesson Continue
------------------------	--------------------------------------	--

- d. A list of collected samples available to ship to the selected repository will appear. Verify that samples listed are the samples you are ready to ship.
 - i. To remove from list samples that are not ready to be shipped, check the box next to the sample and click "Delete". Those samples will be deleted from that list and their status will be retained as "collected".

Site:

	Sample ID	Collected On	Site Label	Subject Label	Sample Label
<input type="checkbox"/>	18908	09/03/2004	T	T1128	Aliquot - 1
<input type="checkbox"/>	18909	09/03/2004	T	T1128	Aliquot - 2
<input type="checkbox"/>	18913	09/03/2004	T	T1129	Aliquot - 1
<input type="checkbox"/>	18914	09/03/2004	T	T1129	Aliquot - 2
<input type="checkbox"/>	18918	09/23/2004	T	T1130	Aliquot - 1
<input type="checkbox"/>	18919	09/23/2004	T	T1130	Aliquot - 2

- e. When the list is accurate, Print Manifest report by clicking "Print".
- f. Press "Ship" button ****Have your Fed-EX shipping bill filled out****
 - i. Enter FedEx shipment number

Explorer User Prompt

Script Prompt:
Enter FedEx Tracking Number

	Sample ID	Collected On	Site Label	Subject Label	Sample Label
<input type="checkbox"/>	18908	09/03/2004	T	T1128	Aliquot - 1
<input type="checkbox"/>	18909	09/03/2004	T	T1128	Aliquot - 2
<input type="checkbox"/>	18913	09/03/2004	T	T1129	Aliquot - 1
<input type="checkbox"/>	18914	09/03/2004	T	T1129	Aliquot - 2
<input type="checkbox"/>	18918	09/23/2004	T	T1130	Aliquot - 1
<input type="checkbox"/>	18919	09/23/2004	T	T1130	Aliquot - 2

- g. Click "OK". A confirmation screen will appear telling you that your samples' status has been changed in the system from "collected" to "shipped". An email will be sent to the DCC and the Repository that has a link to the shipping manifest and tracking number.

Site:

PEGHC@umich.edu, darnms@umich.edu, jbonner@med.umich.edu

Samples marked as Shipped!

[Click Here To Return Home](#)

- h. When you click on the “Samples” button for that subjects’ ID, you’ll see that the status has changed to “Shipped”

Current User: Steve Middlekauff [Logout]
Current Study: A2COH
Current Site:
[Demo Web Pages](#)

Current Subject: [T1130](#)

[View Subject Samples](#) | [Update Samples](#) | [Add Samples](#) | [Samples Report](#) | [Mole Query](#) | [To Lots](#) | [Storage Units](#)

Sample Type	Date Received	Sample Label	Sample Status	Quantity	
Serum (18918)		Aliquot - 1	SHIPPED	1	Sample Record Print Barcode Child Samples (0)
Serum (18919)		Aliquot - 2	SHIPPED	1	Sample Record Print Barcode Child Samples (0)
Whole Blood (18916)			COLLECTED	2	Sample Record Print Barcode Child Samples (0)

5. Other Reporting Functionality

- a. In addition to viewing sample status at a site-specific level, as described above, you can also view sample and form status on a subject level.
- b. Click on the “Subject Status Report” in the drop-down box next to the subject’s PHI button

Current User: Peg Hill-Callahan [Logout]
Current Study: A2COH
Current Site:
Study Programs:
[Demo Web Pages](#)

Label	Last Name	First Name	Med. Rec. No.	Samples	Enter Data	View Data	Discrepancies	Edit Data	View PHI	
R1106				<input type="text" value="247"/>	<input type="text" value="128"/>	<input type="text" value="2"/>		<input type="text" value="2"/>	<input type="text" value="PHI"/>	<input type="text" value="Subject Status Report"/>

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- c. A new window will open up showing you the subject's site and ID number with a series of folders and associated dates. Click on the "+" next to the time point for which you want to review the status of forms and samples.



- d. Open the Forms or Samples folder and you can see the status of the pertinent items. Forms are shown as either NotEntered or ENTERED. Sample status is either: Pending, Collected, Shipped or Received:



8. Shipping instructions to the NIDDK Biosample repository (not for whole blood)

Shipment Schedule

Chicago/New York	→	First Monday of each month
Denver/Philadelphia	→	Second Monday of each month
Virginias/UNC	→	Third Monday of each month
San Francisco/Los Angeles	→	Fourth Monday of each month

Frozen sera and liver tissue will be batch shipped to the NIDDK Biosample Repository every month. All shipments should be sent on Monday or the first workday of the week. The repository will supply shipping labels, cryovial boxes, and boxes for shipment. The DCC will supply the cryo vials and barcode labels for the vials.

Exception: Whole blood for cell lines will be shipped immediately to the Rutgers University facility (Genetics Repository).

When ready to ship frozen storage vials, place the vials in a cryo tube box. Each cryo tube box can hold up to 81 (100) samples. All specimens should have been labeled with the pre-printed barcode and all institutional identifiers removed. A shipping manifest form should be printed that lists each sample being shipped.

Make a copy of the manifest: one copy should be sent with the specimens and the other copy should be placed in the subject's research folder.

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Follow all instructions that you receive from the NIDDK repository. Assemble the Medium Dry Ice Shipper according to those instructions. Note the following steps that are described:

1. Place the specimen (cryovial) box and the absorbent strip inside the inner leak proof poly (plastic) bag. (Only one box in each poly bag.)
2. Place the poly bag inside the Tyvek envelope; remove the cover over the adhesive; and seal the flap,
3. Stack up to 4 Tyvek envelopes in the middle of the Styrofoam cooler.
4. Fill the remainder of the space with dry ice.
5. Put the lid on the cooler and place one copy of each shipping manifest (there will be several manifest for each shipment) on top of the cooler lid.
6. Close and tape the outer cardboard box.
7. Stick the label 'Diagnostic Specimens' and a separate address label on the top of the box in the upper right corner.
8. Stick the dry ice label on the top of the box in the upper left hand corner. Enter the weight of the dry ice as 4 kg.
9. Use the pre-printed Fed Ex air bill to ship the specimens to the McKesson/NIDDK Biosample Repository. Fill in Section 1, leaving the "Sender's Fed Ex account number" blank. In Section 7 enter the total weight of the package and a declared value if it is greater than \$100. Place the airbill in the document pouch; remove the larger/lower section of backing and attach it to the TOP of the box. Do NOT seal the pouch.
10. Call Federal Express at 1-800-GO-FEDEX. Give the account number shown in Section 7, Payment, of the pre-printed FedEx Air Bill. FedEx will dispatch a courier to pick up the package.

The address for shipments is:

Rich Frome
McKesson Bioservices
628 Lofstrano Lane
Rockville, MD 20850

All shipments will be sent frozen. Add enough dry ice to ensure shipment will stay frozen overnight (Max wt is 5 lbs). Check to ensure that the box is properly labeled and package according to the shipping policy (see shipping guidelines).

BioDBx will automatically send a message to the DCC and the repository when shipments are sent.

9. NIDDK Repository – Specimen Tracking

Specimen Arrival:

Once specimens have arrived at the Biosample Repository, they will immediately be scanned into the database and the repository will send a notice to the site confirming arrival. As they are logged into the database they will be checked against the shipping manifest. Any discrepancies will be reported

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back to the originating site for verification. After verification and scanning of the samples, they will be placed into -70°C freezers for storage.

10. Bar Coding

Each sample will be assigned a unique barcode. When the sample is received by the repository, its barcode will be scanned and the database will be updated with the date of receipt and its location in the repository. When the sample is shipped from the repository for analysis, the database will be updated with the date of shipment and the destination.

11. Ordering supplies

11.1 Rutgers Cell & DNA Repository

Notify Emily Gymnich or Jacqueline Sabb that additional kits are necessary. This can be done by email (gymnich@biology.rutgers.edu; sabb@biology.rutgers.edu); fax (1-732-445-1149), or phone (1-732-445-1498). Please include the name of the project (A2ALL) and your NIDDK three-digit site number in all communications.

11.2 McKesson Biosciences Repository

McKesson will provide one shipping container at a time. Up to 3 boxes of vials can be shipped within the container. If additional containers are needed, notify Rich Frome, the PI, via email (Rich.Frome@McKessonBio.com), or Heather Higgins, Assistant PI, at NIDDKrepository@mckessonbio.com or call her mobile phone, 240.793.0353. The repository will be moving shortly and other phone numbers will change. The new phone numbers will be provided when available.

11.3 Vials and vacutainers for blood specimens for McKesson repository

The DCC will provide each site with:

- 2 ml vials for the aliquots
- Bar coded labels for the vials

Please contact the DCC by email (A2ALL-staff@umich.edu) to request additional vials or barcode labels. Include in your request the type and amount of vials/labels that you need. Please allow 2-3 weeks time for shipping; do not wait until your supplies are empty before placing your order.

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APPENDIX

Phlebotomy Form – For Rutgers

Flow sheet for blood sample collection -- For Rutgers

Assembly instructions for international Polyfoam mailers -- For the Bioscience Repository

Assembly instructions for one Polyfoam packer – For Rutgers.

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NIDDK GENETICS INITIATIVE

PHLEBOTOMY FORM-A2ALL

SHIP AT ROOM TEMPERATURE IN SAFETY MAILER & ENCLOSE A COPY OF THIS FORM WITH BLOOD KIT

TO: DR. DOUGLAS FUGMAN/GENETICS
 RUTGERS UNIV./CELL & DNA REPOSITORY
 DIV. LIFE SCIENCES – NELSON LABS
 604 ALLISON ROAD (RM. C120A)
 PISCATAWAY, NJ 08854-8082

FAX: (732) 445-1149
 PHONE: (732) 445-1498

CHECK _____

EMAIL: GYMNICH@BIOLOGY.RUTGERS.EDU
 SABB@BIOLOGY.RUTGERS.EDU
 SELANDER@BIOLOGY.RUTGERS.EDU

FOR RU LAB USE ONLY:
 INITIAL: _____
 YELLOW (ACD) ML: _____
 PURPLE (EDTA) ML: _____
 ID#: _____

FROM (NIDDK SITE): **SITE NUMBER** **NUMBER OF TUBES INCLUDED :**

YELLOW (ACD) TOP TUBES: _____ (PED) _____ (ADULT)
 # PURPLE (EDTA) TOP TUBES: _____ (PED) _____ (ADULT)

NIDDK-A2ALL STAFF: PLACE TUBE LABEL HERE OR COMPLETE BY HAND
 (VERIFY INFO AGAINST INFO ON BLOOD TUBES!!!)

SERVICES
CHECK ALL THAT APPLY

AGE: _____ SEX: M _____ F _____

ALTERNATE ID#: **SUBJECT NUMBER**

NIDDK-ID#: **SITE NUMBER-SUBJECT NUMBER**

CELL LINE

BUFFY COAT (PBMC) _____

DNA _____

PLASMA _____

To Be Completed at Collection Site:

DATE BLOOD DRAWN: _____ - _____ - _____ TIME DRAWN: _____ DRAWN BY: _____
 MONTH – DAY – YEAR 24 HOURS

CONTACT THE RUTGERS CELL & DNA REPOSITORY TO CONVEY PACKAGE TRACKING NO./DATE OF SHIPMENT (SEE BELOW). IF BLOOD IS SHIPPED ON A FRIDAY FOR SATURDAY DELIVERY, NOTIFY RUTGERS AND CHECK FedEx FORM FOR SATURDAY DELIVERY.

EMAILED/FAXED/
 CALL IN TO: _____ RUTGERS UNIVERSITY CELL & DNA REPOSITORY _____ / _____ / _____ _____ (24 HOURS)
 (SEE RUTGERS FAX/PHONE #S ABOVE) DATE TIME

PACKAGE TRACKING #: _____ (CHECK SATURDAY DELIVERY ON DELIVERY FORM IF APPLICABLE)

To Be Completed by Rutgers University Cell & DNA Repository

PRIOR NOTIFICATION REC'D: YES _____ NO _____ - IF YES, DATE/TIME _____ / _____ / _____ _____ AM/PM
 CONFIRMATION OF RECEIPT OF BLOOD
 SAMPLE TO NIDDK SITE SENT BY: _____ DATE _____ / _____ / _____

**A2ALL STUDY
FLOW SHEET FOR BLOOD SAMPLE COLLECTION
FOR NIDDK GENETICS INITIATIVE AT RUTGERS UNIVERSITY**

- 1) Complete and attach bar code labels to the tubes. **DO NOT write the patient's name or any other personal identification information (e.g. SS#, DOB) on the tubes.**
- 2) Collect blood specimen in the appropriate tubes: three 8.5ml ACD (yellow top) tubes for each recipient or donor. **Be sure to invert each tube gently 6 times to mix blood with additives and keep them at room temperature.**
- 3) Double check NIDDK ID #, verify that ID information on tube matches that on the enclosed NIDDK Phlebotomy Collection Form.
- 4) Check services required for blood sample. Date and sign the NIDDK Phlebotomy Collection Form in the TO BE COMPLETED AT COLLECTION SITE section.
- 5) Package the blood tubes in the safety mailer following the enclosed instructions. Be sure to seal the Styrofoam container with the red tape (water resistant).
- 6) Place the collection form (NIDDK Phlebotomy Collection Form) in the mailer box outside of the plastic bag. Tape cardboard box closed when assembly is complete.
- 7) Use the enclosed Fed Ex shipping label to ship the sample to the Rutgers University Cell Repository. Be sure shipping label is marked for priority overnight delivery.
- 8) For routine shipments be sure the outside of the box is labeled "Diagnostic Specimen Packed in Compliance with IATA Packing Instruction 650."
- 9) **Call Federal Express, 1-800-GO-FEDEX (1-800-463-3339), and a courier will be dispatched to pick up the samples. Be sure to give Fed Ex the Zip Code of the PICKUP address, not that of the destination.**
- 10) **Notify Emily Gymnich and Jacqueline Sabb at the Rutgers University Cell and DNA Repository that blood is being shipped and provide the Federal Express tracking number _____ and NIDDK ID # _____. This can be done by email (gymnich@biology.rutgers.edu; sabb@biology.rutgers.edu), fax (1-732-445-1149), or phone (1-732-445-1498). THIS IS DONE AUTOMATICALLY BY BioDBx**

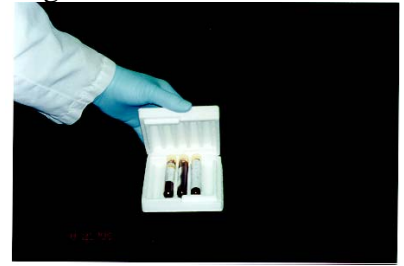
Feb. 2, 2005

ASSEMBLY INSTRUCTIONS FOR INTERNATIONAL POLYFOAM MAILERS

READ ALL INSTRUCTIONS THOROUGHLY BEFORE STARTING ASSEMBLY

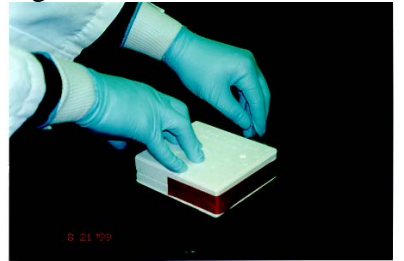
- 1) Place the labeled tubes into the small Styrofoam insert using the same insert that the empty tubes came in (Fig. 1). DO NOT tape the top of the blood tubes.

Fig. 1



- 2) Tape the small Styrofoam insert closed. Peel the backing from one piece of red waterproof tape and begin sealing the Styrofoam lid to the body. Then peel the backing from the second piece of tape and continue sealing the insert, overlapping the first piece of tape about two inches on both ends (Fig. 2).

Fig. 2



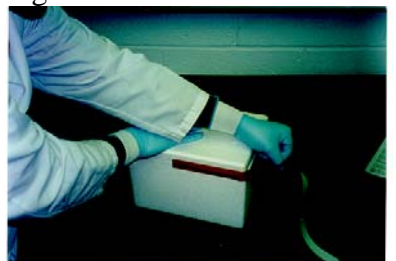
- 3) Place the small Styrofoam insert into the press-lock plastic bag. Seal the bag and place it into the large Styrofoam mailer (Fig. 3). Fill the mailer with packing material to prevent disturbing the blood tubes during shipment. Include a copy of the completed Data Collection Form inside the large Styrofoam mailer.

Fig. 3



- 4) Tape the large Styrofoam mailer closed. Peel the backing from one piece of red waterproof tape and begin sealing the Styrofoam lid to the body. Then peel the backing from the second piece of tape and continue sealing the mailer, overlapping the first piece of tape about two inches on both ends (Fig. 4).

Fig. 4



- 5) Slide the Styrofoam mailer into the corrugated carton (Fig. 5) and seal the carton with packing tape. Place the Federal Express International shipping form and any other necessary documents (i.e. International Invoice Form and Declaration Statement on Rutgers letterhead) on the outside of the carton and contact Federal Express FOR PICKUP.

Fig. 5

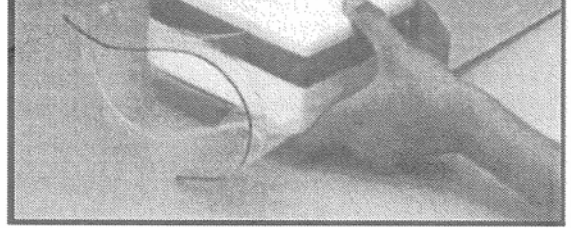


6) Slide the Safety Mailer and open press-lock bag into the corrugated carton (Fig. 4). Then seal the press-lock bag, close the carton using the locking tabs, and place sealing tape (not included) over them.

POLYFOAM Packers

Division of Tuscarora Incorporated
Part of SCA Global Packaging

2320 Foster Ave, Wheeling, IL 60090-6572
800-323-7442 • 847-632-9600 • FAX 847-398-0653
www.polyfoam.com



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LIT 127-08/02

Feb. 2, 2005

THE STATE UNIVERSITY OF NEW JERSEY

RUTGERS

Department of Genetics - Cell & DNA Repository

Nelson Biological Laboratories - Room C 120A
604 Allison Road • Piscataway • New Jersey 08854-8082
Phone: 732-445-1498 Fax: 732-445-1149

DECLARATION STATEMENT

The contents of this package are as follows:

- Human whole blood specimens in sealed Vacutainer collection tubes.
- These human blood samples have not been exposed to any animal derived materials such as products derived from livestock or avian disease agents.
- This material is not of tissue culture origin.
- These blood samples are not known to be infectious or contagious.
- **Diagnostic specimens packed in compliance with packing instruction 650.**

These samples are being shipped to the Rutgers University Cell Repository for investigational purposes funded under the National Institute of Diabetes and Digestive and Kidney Diseases Genetics Repository (Contract #N01-DK-3-2610). Samples are packed in approved blood mailers and are perishable. Subjects are being collected for genetic analysis and are not known to be infectious. **Please do not delay.**

These samples are for investigational purposes only and are not required to be screened for HIV or Hepatitis B or C.

If you have any questions or concerns, please contact Dr. Douglas Fugman.

Sincerely,

Dr. Douglas A. Fugman, Ph.D.
Managing Director
Rutgers University Cell & DNA Repository
Phone: 732-445-7024; 732-445-1498
Fax: 732-445-1149

A. Product Description

RNAlater® is an aqueous, non-toxic tissue storage reagent that rapidly permeates tissue to stabilize and protect cellular RNA in situ in *unfrozen* specimens. Tissue pieces are harvested and immediately submerged in RNAlater for storage without jeopardizing the quality or quantity of RNA. RNAlater eliminates the need to immediately process tissue specimens or to freeze samples in liquid nitrogen for later processing. The figures below show 2 common experiments using RNA isolated from RNAlater-preserved samples.

RNAlater preserves RNA in tissues for up to 1 day at 37°C, 1 week at 25°C, and 1 month or more at 4°C. Tissues can also be stored at -20°C or at -80°C long-term.

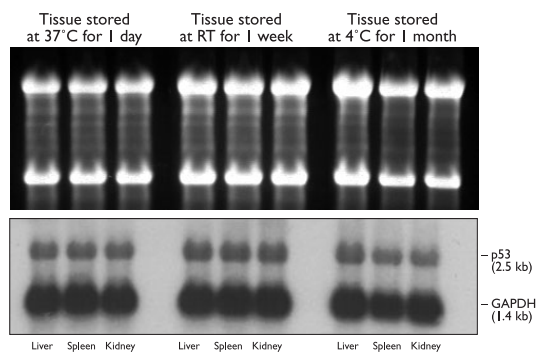


Figure 1. RNA from Tissue Stored in RNAlater

RNA was extracted from mouse tissues stored in RNAlater as shown. The top panel is an ethidium bromide-stained denaturing agarose gel; the bottom panel shows a Northern blot.

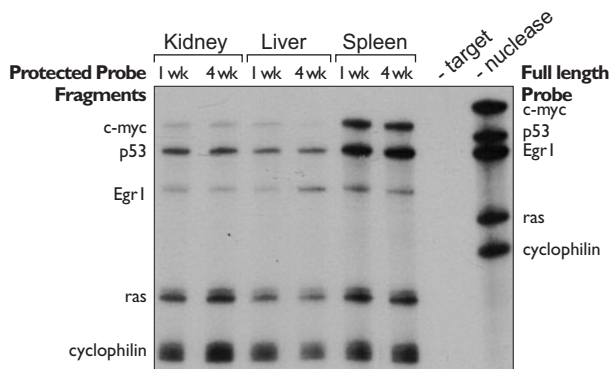


Figure 2. mRNA profiles of mouse tissues stored in RNAlater

The indicated mouse tissues were stored in RNAlater for 1 or 4 weeks at 4°C. RNA was isolated from each tissue and analysed using Ambion's RPA III™ kit. 10 µg of RNA was hybridized with a mixture of 5x10⁴ cpm of each of 5 antisense probes. The gel was exposed to film for 4 hours at -80°C with an intensifying screen.

Storage and Stability

Store RNAlater at room temperature. It is guaranteed for 6 months from the date received.

If any precipitation of RNAlater is seen, heat the solution to 37°C and agitate to redissolve it.

What materials have been tested in RNAlater?

RNAlater has been extensively tested on tissues from several vertebrate species. These include brain, heart, kidney, spleen, liver, testis, skeletal muscle, fat, lung and thymus. RNAlater is also effective for *E. Coli*, *Drosophila*, tissue culture cells, white blood cells, and some plants.

Will RNAlater work with my RNA Isolation Kit?

RNAlater is compatible with most RNA isolation methods. Specifically, we have used RNAlater-preserved samples with TRI Reagent®1, and all of Ambion's RNA isolation kits and reagents, including: RNAwiz™ (one-step disruption/separation reagent), ToTALLY RNA™ (guanidinium isothiocyanate disruption, acid phenol extraction), RNAqueous™ (phenol-free, glass fiber filter binding), PARIS™ (Protein and RNA Isolation System), mirVana™ miRNA Isolation Kit (glass fiber filter microRNA isolation), and MicroPoly(A)Pure™ (direct isolation of poly(A) RNA from guanidinium lysate).

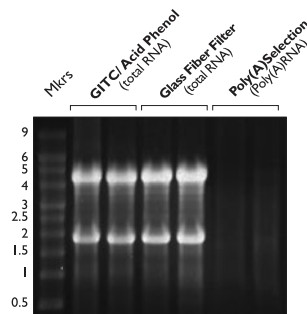


Figure 3. RNA isolated from tissue stored in RNAlater using different isolation methods

Whole mouse hearts and livers were dissected, and placed in RNAlater, in which they were stored for 3 days at 4°C. RNA was isolated from equal mass amounts of each tissue using the indicated Ambion kits. RNA (5 µg) was run on denaturing agarose, stained with ethidium bromide.

Can genomic DNA be obtained from RNAlater-stored samples?

Yes, contact Technical Service and request a protocol.

Can protein be obtained from RNAlater-stored samples?

Yes, proteins are also preserved in RNAlater. Storage in RNAlater will denature proteins, therefore total protein obtained from samples stored in RNAlater will be competent for applications such as Western blotting or 2D gel electrophoresis, but will not be suitable for applications that require native protein.

B. How to use RNAlater

Use RNAlater with fresh tissue only, do not freeze tissue before immersion in RNAlater. Simply cut tissue samples to a maximum thickness of 0.5 cm in any 1 dimension, as long as samples are ≤0.5 cm thick, their size of the other dimensions is not important. Place the fresh tissue in 5 volumes of RNAlater, and store as indicated for the desired temperature.

**NOTE**

Ambion offers RNAlater®-ICE (Cat #7030) as a salvage pathway to recover tissues that have already been frozen. RNAlater-ICE renders frozen tissues pliant enough for homogenization while maintaining low temperatures to protect the RNA from degradation.

1 TRI Reagent, and TRIzol are registered trademarks of Molecular Research Center Inc.

Animal Tissue	RNAlater does not dissolve or disrupt the structure of tissue samples, thus tissue that has been equilibrated in RNAlater can be removed from the solution, sectioned into smaller pieces, and returned to RNAlater if desired. Small organs such as rat liver, kidney and spleen can be stored in RNAlater whole.
Plant Tissue	Many plant tissues can be simply submerged in 5 volumes of RNAlater for storage. We have successfully isolated intact RNA from tobacco leaf explants, entire arabidopsis and alfalfa seedlings, and from potato shoot tips. Plant tissues that have natural barriers to diffusion such as waxy coatings on leaves will probably require disruption to allow RNAlater access to the tissue.
Tissue Culture Cells	Pellet cells according to the protocol followed by your laboratory. Wash to remove the culture medium (e.g. with PBS). Resuspend the cells in a small volume of PBS, then add 5 to 10 volumes RNAlater.
Blood and Plasma	White blood cells can be effectively preserved in RNAlater when separated from the red blood cells and sera and treated as tissue culture cells. RNAlater will preserve RNA in anticoagulated whole blood, sera, and plasma; however, it may be difficult to recover cells or viral particles by centrifugation due to the density of RNAlater. See the RiboPure™ Blood Kit (Ambion Cat #1928) manual for specific instructions on use of RNAlater with whole blood.
Bacteria	RNAlater is bacteriostatic; although bacteria do not grow in RNAlater, the cells remain intact. <i>E. coli</i> stored in RNAlater for 1 month at 4°C are intact and yield undegraded RNA.

C. Storage of Samples in RNAlater

Storage at -80°C

Recommended for archival storage. Incubate samples at 4°C overnight, then remove them from RNAlater before storage at -80°C. For tissue culture cells, do not remove the RNAlater, simply freeze the whole solution. The cell types we have tested do not lyse when frozen at -80°C in RNAlater. Samples can subsequently be thawed at room temperature and refrozen without affecting the amount or the integrity of the recoverable RNA.

Storage at -20°C

Recommended for archival storage. Incubate samples at 4°C overnight, then transfer to -20°C. Samples will not freeze at -20°C, but crystals may form in the storage buffer; this will not affect subsequent RNA isolation. Samples can subsequently be thawed at room temperature and refrozen without affecting the amount or the integrity of the recoverable RNA.

Storage at 4°C

Ambion sees no evidence of RNA degradation in samples stored at 4°C for up to 1 month.

If Refrigeration is not Possible:

Place the samples in as cool an environment as possible. If ambient temperature is above 25°C, incubate samples in RNAlater on ice for a few hours if possible before storing at ambient temperature.

Storage at 25°C

RNA isolated from samples stored at 25°C for one week is intact. In our experience, RNA from samples stored at 25°C for two weeks appears slightly degraded (marginally acceptable for northern analysis, but still of sufficient quality for nuclease protection assay or RT-PCR analysis).

Storage at 37°C

RNA isolated from samples stored at 37°C is intact after a 24 hour incubation, but is partially degraded after a 3 day incubation.

D. RNA Isolation from Material in RNAlater

1. Removing Samples from RNAlater

RNAlater can be discarded down the sink with running water.

Tissue

Tissues that have been stored in RNAlater should be removed from the storage solution with sterile forceps, and submerged in RNA isolation lysis solution. Tissue homogenization should be rapid once the tissue is in lysis/denaturation solution.

Cells

There are two options for isolating RNA from cells stored in RNAlater, the RNAlater can be removed, or the RNA can be extracted from the mixture of cells and RNAlater.

- Removal of RNAlater

Our experience is that cells become much less fragile when stored in RNAlater and can be centrifuged at high speed without lysis. We have successfully centrifuged cells at 5000 x g without loss. Since different cells may respond differently to this force, we suggest you try pelleting a non-valuable sample first to confirm that you can recover your cells this way. An alternative is to dilute the RNAlater by 50% immediately before centrifugation with cold PBS (or other buffered solution) in order to reduce the density of the solution.

- RNA extraction from cells in RNAlater

Alternatively, we have used one-step disruption/extraction solutions (e.g. RNAwiz™, and TRI Reagent) to purify RNA from cells that have not been removed from RNAlater. This can be done by adding ten volumes of the one-step solution to the cell mixture, and proceeding normally. When Ambion's RNAwiz™ is used in this way, it may be necessary to dilute the aqueous phase before the RNA precipitation step, see below for more information.

2. Tips for RNA Isolation

Glass fiber-based extraction

Using glass fiber filter-based RNA isolation kits, it may be necessary to use a centrifuge to push lysates through the filter as opposed to using a vacuum manifold.

One-step disruption/extraction solutions

When using one-step RNA isolation products such as TRIzol® (or TRI Reagent) on RNAlater-preserved samples, occasionally the aqueous phase is cloudy. If this occurs, simply continue the procedure, following the manufacturer's instructions. Cloudiness of the aqueous phase does not affect the quantity or quality of the RNA obtained.

With Ambion's RNAwiz™, there may be a problem getting the aqueous phase to mix with isopropanol at the precipitation step because of RNAlater carryover. If this occurs, simply add a mixture of 50% water, 50% isopropanol until the solution becomes clear and the two phases mix. The amount of water/isopropanol required will depend on how much RNAlater was carried over; if the sample was mostly RNAlater, as much as an equal volume may be needed.

E. RNAlater Specifications

Quality Assurance:

RNAlater undergoes quality assurance testing to verify that its composition is invariant from lot to lot.

Safety:

This product is a proprietary solution whose chemical, physical, and toxicological properties have not been thoroughly investigated. See the following MSDS for more information.

F. RNAlater® Material Safety Data Sheet

Physical data

Appearance and odor	clear liquid, slightly viscous
Boiling point	n/a
Solubility in H ₂ O	soluble

Fire and explosion hazard data

Flash point	n/a
Flammable limits in air	n/a
Extinguishing media	water, CO ₂ , foam, dry chemical (Use any means suitable for extinguishing surrounding fire)
Special fire fighting	Wear self-contained breathing apparatus and protective clothing.
Fire/explosion hazards	Irritating and/or toxic gases or fumes may be generated by thermal decomposition or combustion.

Health hazard data

Effects of overexposure	Acute overexposure may cause irritation to eyes, skin, and respiratory tract.
Emergency first aid	Flush affected area with copious amounts of water. Irrigate eyes and skin for ≥15 minutes. Contact physician if irritation occurs due to salt content.

Reactivity data

Stability	stable
Incompatibility	n/a
Haz. Decomp. Products	n/a
Hazardous Polymerization	n/a

Spill or leak procedures

If released or spilled	Ventilate area. Absorb spill with inert material. Place in container with a lid. Wash spill area after cleanup.
Waste disposal method	Dispose of according to federal, local and state regulations.

Special protection and precaution information

Respiratory protection	Not expected to require personal respirator usage. (Use NIOSH approved respirator if necessary)
Ventilation	Not expected to require special ventilation
Precautionary labeling	none
Handling and storage considerations	Laboratory aprons and gloves. Do not store in aluminum or copper containers. Keep tightly closed in a cool, dry place.

This bulletin is for your guidance and is based upon information and tests believed to be reliable. Ambion makes no guarantee of the accuracy or completeness of the data and shall not be liable for any damages thereto. The data are offered solely for your consideration, investigation, and verification. These suggestions should not be confused with either state, municipal, or insurance requirements, or with national safety codes and constitute no warranty. Any use of these data and information must be determined by the user to be in accordance with applicable federal, state, and local regulations.

Specimen Handling

A2ALL

Repository Info

- **Rutgers Genetics Repository** – collect a whole blood sample from donors and recipients at enrollment. This blood has to be shipped at room temperature the same day it's drawn.
- **McKesson Biosample Repository** – send samples of serum and tissue from various timepoints in the protocol, or in an event-driven encounter.

Supplies

- **DCC provides:**
 - pre-printed bar-coded sample labels to each site on a regular basis.
 - 2 ml cryovials for serum aliquots.
- **Rutgers provides:**
 - phlebotomy blood collection tubes
 - shipping kit.
- **ThermoFisher (McKesson) provides:**
 - shipping kit (including dry ice containers).
- **Your site will provide SST tubes and needles for blood collection**

Rutgers Genetics Repository Information

A2ALL

What Rutgers needs from you...

- Prior notification of all incoming whole blood samples
- Full blood tubes from Phlebotomists
- Blood tubes must be inverted 6 times to assure solution within tube properly mixes with blood
- Always keep blood at room temperature

DO NOT REFRIGERATE

- NEVER put blood into FedEx drop boxes
- If drawing blood on Friday, mark for Saturday delivery or if on Saturday mark for Monday delivery
- Samples can be received Monday through Saturday

A2ALL

Whole Blood Collection Steps

- Label tubes provided in Rutgers shipping kit
- Collect blood specimens in the labeled tubes
- Fill out the appropriate portions of the Phlebotomy Collection Form
- Package the blood tubes in the safety mailer
- Place the collection form in the mailer box outside of the plastic bag

Collection Steps Cont...

- Use the provided FedEx shipping label
- “Diagnostic Specimen Packed in Compliance with IATA Packing Instruction 650”
- Call Federal Express, 1-800-GO-FEDEX (1-800-463-3339), and a courier will be dispatched to pick up the samples.

NEVER PUT BLOOD KITS INTO A FEDEX DROP BOX!

Labeling Blood Tubes

- Absolutely NO personal identifiers should be on tubes, i.e. S.S.N, names, D.O.B., etc.
- All tubes must have a Study ID# (NIDDK#) to be accepted
- The Study ID# must begin with the site number, a hyphen, then a unique sample number
- If labels are being used, apply lengthwise on tube over original Vacutainer label, do not wrap around
- Leave at least a ¼ inch window along axis of tube for Rutgers technicians to measure volume & see separation of layers
- For all tubes labels should not cover rubber top

Applying Labels to Adult Tubes

Correct



Incorrect



FROM (NIDDK SITE):

SHIPMENT TO INCLUDE BLOOD
SAMPLES FOR CELL LINES

YELLOW TOP TUBES: _____

NIDDK STAFF: PLACE TUBE LABEL HERE OR COMPLETE BY HAND

(VERIFY INFO AGAINST INFO ON BLOOD TUBES!!!)

SEX: M ___ F ___

AGE: _____

ALTERNATE ID#: _____

NIDDK-ID#: _____

TO BE COMPLETED AT COLLECTION SITE:

DATE BLOOD DRAWN: _____ - _____ - _____ TIME DRAWN: _____ (24 HOURS) DRAWN BY: _____

CONTACT THE RUTGERS CELL & DNA REPOSITORY TO CONVEY PACKAGE TRACKING NO./DATE OF SHIPMENT (SEE BELOW). IF BLOOD IS SHIPPED ON A FRIDAY FOR SATURDAY DELIVERY, NOTIFY RUTGERS AND CHECK FEDEX FORM FOR SATURDAY DELIVERY.

EMAILED/FAXED/

CALL IN BY: _____

(SEE RUTGERS FAX/PHONE #S ABOVE)

_____/_____/_____
DATE

_____/_____/_____
TIME A/M/P/M

PACKAGE TRACKING #: _____

(CHECK SATURDAY DELIVERY ON DELIVERY FORM IF APPLICABLE)

A2ALL

Proper Packaging of Rutgers Samples

- Packaging instructions are enclosed in every kit
- Place tubes into Styrofoam mailer with labels that have the NIDDK ID# facing down
- Secure tubes in place with lab tape.

Correct



Incorrect



Key NIDDK Contact Personnel at Rutgers

- **Dana Witt** – Communications Director
witt@biology.rutgers.edu
- **Dale Hayward** – Communications Coordinator
heyward@biology.rutgers.edu Tel: (732) 445-1498
- Please note that you can use the following email address to reach all staff at the Rutgers office. You may place shipping kit orders through this email:
commstaff@biology.rutgers.edu
 - Kits come 25 to a case
 - Kits should be requested at least 4 weeks before current supply runs out in order to ensure timely delivery

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ThermoFisher Biosample Repository (McKesson)

- All samples, except for Rutgers whole blood specimens, are shipped to ThermoFisher (McKesson)
 - Serum aliquots (Frozen)
 - Liver Tissue (Ambient & Frozen)
- Shipping Kits are provided by the Repository.

Aliquot Samples

- Aliquot serum from SST into cryovials
- 4.0ml of serum should be available to be divided into ten 400 μ l aliquots
- If there is less volume, fill as many vials with 400 μ l as possible
- Do NOT divide equally into the vials
- ****Barcode Scan in BioDBx****
- Place **labeled** cryovials with aliquots in -70°C freezer
- Stored samples will be batch-shipped to McKesson each month (**see schedule**)

A2ALL

Collecting Liver Tissue

- Local arrangements for specimen collection from the OR will apply.
- Each biopsy is cut into thirds; 2 in RNALater (then frozen), 1 in paraffin block (ambient)
- The presence of a study coordinator in the OR may expedite both the labeling of the specimen and its prompt handling

Shipping Samples to the Biosample Repository

Shipping Schedule

- Chicago/New York - First Monday of each month
- Colorado/Penn – Second Monday of each month
- Virginias/UNC – Third Monday of each month
- UCLA/UCSF – Fourth Monday of each month



Sample Shipping (cont'd)

- **Print a manifest from BioDBx**
- **Use the appropriate kit (ambient or frozen)**
- **Pack the specimens according to the instructions included with the shipping kit**
- **Enter the weight of the dry ice as 4kg**
- **Put the appropriate stickers on the box**
- **Use the pre-printed FedEx airbill.**
- **Call Federal Express (1-800-GO-FEDEX) and FedEx will dispatch a courier to pick up the package**

NIDDK Biosample Repository Shipping Address

**Fisher BioServices
20301 Century Blvd.
Bldg. 6, Suite 400
Germantown, MD 20874**

A2ALL

NIDDK Biosample Repository Supply Orders

**Please use our group email address to
order supplies and send shipment
notifications:**

Bio-NIDDKRepository@thermofisher.com

A2ALL

Other Contact Information

Heather Higgins

Principal Investigator

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Heather.Higgins@thermofisher.com

Sandra Ke

Assistant Principal Investigator

Office: 240-686-4702

Sandra.Ke@thermofisher.com

Clifford Snell

Contract Administrator

Office: 240-686-4706

Clifford.Snell@thermofisher.com

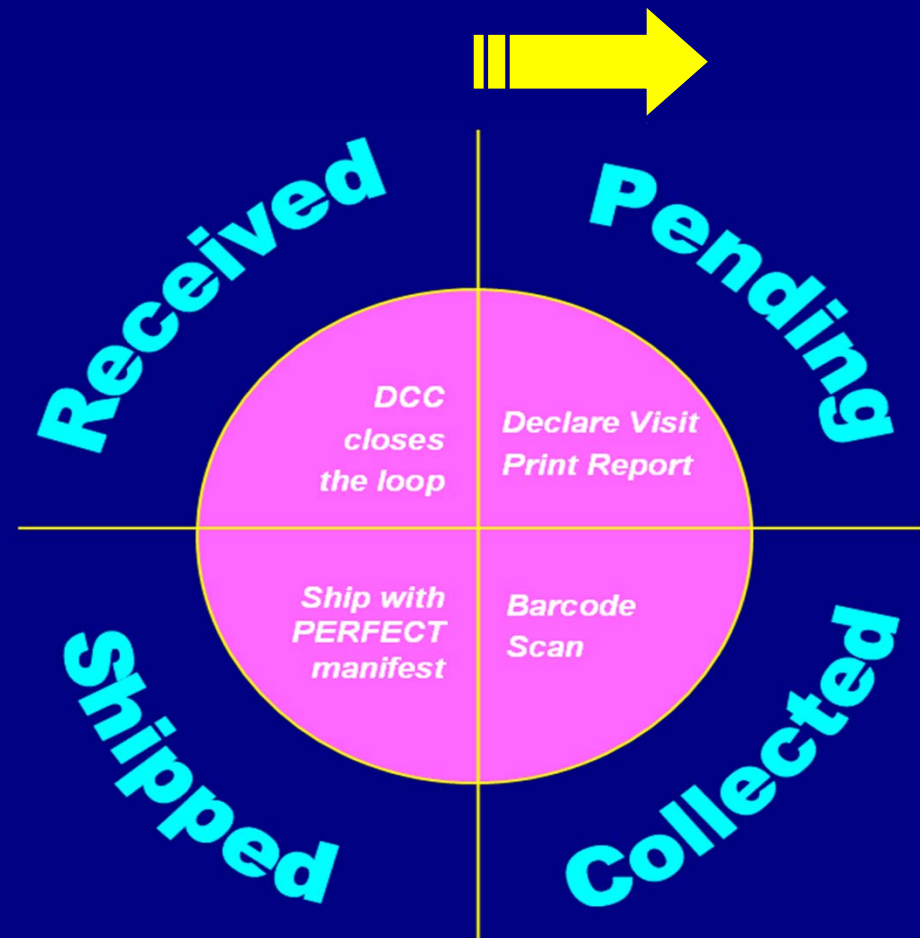
A2ALL

Sample Handling in BioDBx

A2ALL

Cohort Study Sample Handling Process

The Cycle



A2ALL

Cohort Study Sample Handling Process

The Cycle



BioDBx Labels

- Labels are printed by the DCC and sent out to the sites via FedEx.
- When enrolling a subject, BioDBx will assign the next available subject number to your new enrollee, and the labels for this subject should already be at your site.
- When you are ready to collect a sample, you will go into BioDBx and associate the pre-printed labels with the subject, visit type and sample type.

Time points for which there are no labels

- Pre-printed labels only go up to Year 5 (Month 60)
- Some subjects (Cohort Lite, Former Retro, etc.) will have follow-up beyond these time points.
 - For these subjects, unused labels can be used for later time points.

Label Change Procedures

- Declare visit on PHI page
- Write correct time point on label
- Email Abby (abbysmit@umich.edu) with the following information:
 - Subject ID #
 - Original time point from label
 - Actual time point from sample
 - Sample type (serum vs. bx)
 - Sample numbers

Cohort Study Sample Handling Process

The Cycle



Logging Samples in BioDBx

- Scanning labels
- Scanning printed barcode report

A note about the importance of logging samples

- **If you do not log samples they will not move to the next stage of the cycle and you will not receive credit for having collected them.**
- **The Steering Committee regularly reviews sample handling status, so it is important that the status of you samples remains up to date to insure accurate reporting.**

Cohort Study Sample Handling Process

The Cycle



A2ALL

Electronic Shipping

- **Preparing your manifest**
 - Make sure your manifest matches what's in your box.
 - * *Note: If you back out of your manifest all deleted samples will return.*
 - Have your FedEx tracking number on hand before preparing your manifest.
- **Pressing the “Ship” button**
 - This is the point of no return so make sure your manifest is correct.
 - BioDBx will automatically generate an email to the repository, the DCC, and the shipper, that the samples have been sent.

Things to Know about Shipping

- **Unlogged samples will not show up on your manifest.**
- **When they receive samples, the repository checks the manifest against the box. Any discrepancies must be reconciled.**
- **The database can only handle so many samples per manifest. If you have too many samples built up on your manifest, you will not be able to open it. Please ship regularly to avoid this problem.**

Your Responsibilities in Accurate Sample Handling

- Declaring visits
- Logging samples
- Accurate electronic shipping
- Shipping regularly
- Informing the DCC of label changes

Cohort Study Sample Handling Process

The Cycle



When to Call the DCC

Please feel free to call us whenever you have any questions about BioDBx and sample handling.

Abby and Monique
(734) 998 6580

abbysmit@umich.edu

mlowe@umich.edu

A2ALL REPOSITORY GUIDELINES

SERUM and TISSUE SAMPLE PREPARATION

Feb. 2, 2005

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1. Center numbers for the Repository

Each site has been assigned a center number that must be used when shipping samples to the repository. A2ALL sites are identified uniquely by a two digit number listed in the table below:

PI	Site	Site	NIDDK Site Number
Emond	New York	Columbia Presbyterian	310
Abecassis	Chicago	Northwestern University	311
Shaked	Philadelphia	University of Pennsylvania Health System	312
Trotter	Denver	University of Colorado Health System	313
Ghobrial	Los Angeles	University of California, Los Angeles	314
Freise	San Francisco	University of California, San Francisco	315
Fair	Chapel Hill	University of North Carolina	316
Berg	Charlottesville	University of Virginia Health System	317
Fisher	Richmond	Virginia Commonwealth University	318

2. Specimen Repositories

There are two repositories:

1. NIDDK has contracted with the Rutgers University Cell & DNA Repository (Genetics Repository) to establish cell lines or to extract PBMC's and DNA from whole blood. Whole blood for cell lines, or for DNA and PBMC extraction, will be shipped immediately upon collection to the repository at Rutgers.
2. NIDDK has established a Biosample Repository (McKesson) for long-term storage of blood, tissue specimens and slides (i.e., all samples except the whole blood that is sent to Rutgers University). Samples will be processed as described below, frozen and then shipped via licensed overnight carrier once every month to the NIDDK repository.

All specimens will be labeled with a research study subject identifier and a vial barcode that will include the site number, but will be otherwise de-identified prior to shipment to either location. All samples will be accompanied by a shipping manifest that will describe the content of each vial. Receipt of samples by the repository will be acknowledged to the originating center.

3. Schedule for Specimen Collection

3.1. From the Recipient

Blood and samples from the recipient will be collected at:

- Time of initial evaluation/enrollment
- Quarterly visits pre-transplant (starting from enrollment)
- Transplantation (2 samples)
- Day one post-transplant
- 1 week post-transplant

Feb. 2, 2005

2 week post-transplant

1 month post-transplant

3 month post-transplant

6 month post-transplant

12 month post-transplant

Annually thereafter until study ends

Blood samples should be drawn at the same time as blood is taken for clinical testing or when there is IV access for a clinical procedure.

At each of the above times, draw:

- 15 ml of whole blood in SST vials for serum

At the enrollment visit ONLY, also draw:

- 24 ml of whole blood in three 8 ml ACD vials provided by the Rutgers University Cell & DNA Repository.

Other Specimens: At transplantation tissue samples will be collected on all recipients and liver samples will be collected from HCV positive recipients at selected visits. See section 5.4 for a description of these samples.

3.2. From the Donor

Blood and samples from the donor will be collected at:

Time of initial evaluation/enrollment

Donation surgery (3 samples)

Day one post-transplant

1 week post-transplant

1 month post-transplant

3 month post-transplant

12 month post-transplant

Annually thereafter until study ends

Blood samples from each donor will be obtained, when possible, at the time of consent or at a convenient time during the ongoing clinical evaluation. From each donor, at each visit listed above, draw:

- 15 ml of whole blood in an SST vial for serum

At the transplant visit ONLY, also draw:

- 24 ml of whole blood in three 8 ml ACD vials provided by the Rutgers University Cell & DNA Repository.

Other Specimens: At donation, tissue samples will be collected from all donors. See section 5.4 for a description of these samples.

The processing of the blood samples from the donors is the same as that for the recipient

4. Rutgers University Cell & DNA Repository (RUCDR)

The RUCDR will provide all the supplies (except labels for the vacutainers) that the site needs to collect and ship whole blood to the RUCDR. The RUCDR will ship to each site cartons containing 25 kits.

Each kit will contain a set of three 8.5 ml ACD vacutainer vials. The whole blood must be shipped on the day of collection to the RUCDR.

Each kit consists of:

- a cardboard box that should be used to ship the samples,
- a Styrofoam box containing the vacutainers and packing material
- red, water-proof tape
- a press-lock plastic bag
- instructions
- phlebotomy collection form
- FEDex Airbill

Follow the instructions that are provided. They describe how to:

- Label the vacutainers.
- Collect the sample in the vacutainers that are provided.
- Shake the vacutainers.
- Pack the vacutainers in the boxes.
- Complete the phlebotomy collection form
- Complete the Airbill – note that there is already an account number on it and.
- Call FEDex so the package is picked up that day – do NOT keep the sample overnight.

The RUCDR Phlebotomy Collection Form refers to a NIDDK-ID# and an alternate ID#. The **NIDDK-ID#** is the three digit NIDDK site ID followed by a hyphen followed by the assigned BioDBx sample number.

The **alternate ID number** is a second identifier in case the first is unreadable and this will be the subject ID number. You will need to copy the numbers onto the RUCDR Phlebotomy Collection Form.

4.1. Whole blood for the Rutgers University Cell & DNA Repository

Preparation for immortalized cell lines or DNA extraction

Be sure the following materials are readily accessible in addition to what is needed for plasma handling.

- Recipient or Donor: Three 8.5 ml ACD vials provided by the Rutgers University Cell & DNA Repository.

4.2. Specimen handling for the Rutgers University Cell & DNA Repository

- The Rutgers University Cell & DNA Repository will supply all the blood vacutainer tubes and packaging material to be used.
- **DO NOT write the patient's name or any other personal identification information (e.g. SS#, DOB) on the tubes.**
- Affix the appropriate subject's bar code label onto each vial-note that the three RUTGERS blood collection tubes will all have the same label attached for each patient (same sample number assigned)
- Complete the Phlebotomy Collection Form: The top panel is completed by the RUCDR. The RUCDR Phlebotomy Collection Form refers to a NIDDK-ID# and an alternate ID#. The NIDDK-ID# is the three digit site ID followed by a hyphen followed by the assigned BioDBx sample number. The alternate ID number will be the subject ID number. You will need to copy the numbers onto the RUCDR Phlebotomy Collection Form.
- Collect blood specimen into the three vacutainer tubes.
- After collecting whole blood into the tubes, gently invert the tube 6 times to mix with additives and keep them at room temperature.
- Double check subject ID, verify that ID information on tube matches that on the enclosed NIDDK Phlebotomy Collection Form.
- Date and sign the NIDDK Phlebotomy Collection Form – TO BE COMPLETED IN PHLEBOTOMIST area. *Make two copies of this form – one to be kept in the research file and the second to be sent to the Repository.*
- Package the blood tubes in the safety mailer following the enclosed instructions. Be sure to seal the Styrofoam container with the red water resistant tape.
- Place the NIDDK Phlebotomy Collection Form in the mailer box outside of the plastic bag. Tape the cardboard box closed when the assembly is complete.
- Use the enclosed Fed Ex shipping label to ship the sample to the Rutgers University Cell & DNA Repository. Be sure the shipping label is marked for priority overnight delivery.
- For routine shipments, be sure the outside of the box is labeled "Diagnostic Specimen Packed in Compliance with IATA Packing Instruction 650."
- Update BioDBx with date of sample and bar code labels used-Status = shipped
- **Call Federal Express, 1-800-GO-FEDEX (1-800-463-3339)**, and a courier will be dispatched to pick up the samples.
- **Notify Emily Gymnich and Jacqueline Sabb at the Rutgers University Cell and DNA Repository** that blood is being shipped and provide the Federal Express tracking number(s) _____ and NIDDK ID #(s) _____. This can be done by email (gymnich@biology.rutgers.edu and sabb@biology.rutgers.edu), fax (1-732-445-1149), or phone (1-732-445-1498). **THIS WILL BE DONE AUTOMATICALLY BY BioDBx**

Address: Dr. Douglas Fugman/Genetics

Rutgers Univ. Cell & DNA Repository
Div. Life Sciences-Nelson Labs
604 Allison Road (Rm C120A)

5. NIDDK Biosample Repository (McKesson) and Sample Handling

All samples, except the whole blood for cell lines or DNA, are shipped to the NIDDK Biosample Repository. All shipping materials will be provided by the repository. This includes:

Each shipping kit consists of:

- a cardboard box that should be used to ship the samples,
- a large Styrofoam box
- 3 81-well cardboard vial boxes
- instructions for shipping
- FEDEX Airbill

The DCC will provide each site with:

- 2 ml cryovials for the aliquots
- bar coded shipping labels for the vials (one set for each patient)

5.1. Serum for the NIDDK Biosample Repository

Preparation for Serum Collection

Be sure the following materials are readily accessible before performing venipuncture: All necessary tubes, identified for size, draw, and additive; labels for the tubes.

Recipients and Donors:

- Two 7.5 ml SST tube
- 10 storage cryovials, labeled in advance with supplied patient specific labels-use correct visit and sample type labels

Serum specimen handling:

- Blood will be drawn using two 7.5 ml serum separator tubes (SST) according to each hospital's venipuncture procedure.
- After collection of whole blood into the SST tube, gently invert the tube 8-10 times.
- After mixing, store the SST tube upright at room temperature until centrifugation.
- Blood samples should be centrifuged **within 2 hours** for best results.
- Centrifuge SST tube/blood sample at room temperature (18-25°C) in a horizontal rotor (swing-out head) for a minimum of 10 minutes at 1,100 RCF (Relative Centifugal Force).
- Be sure that there is not any subject identifying material on the cryovials that will be sent to the repository.

Use the 10 labeled cryovials

- Aliquot serum into cryovials

4.0 ml of serum should be available to be divided into ten 400 µl aliquots

If there is less volume, fill as many vials with

400 µl as possible – **do NOT divide equally into the vials**

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- Enter BioDBx and associate the patient specific barcode labels with the sample dates
- Place cryovials with aliquots in -70°C freezer
- Stored samples should be batch shipped every month

5.2. Tissues obtained at surgery or at time of biopsy

Preparation for tissue specimens

For each type of specimen described below, prepare (2 ml vial) vials with patient specific labels:

Tru-Cut needle biopsy tissue core should be divided into three equal pieces.

Have three labeled 2ml cryovials ready-two filled with 1 ml of RNALater and one filled with 1 ml of formalin. Make sure the liquid is not close to the top of vial due to expansion. After the vial is capped and tissue has been placed inside-invert several times to ensure that tissue is completely submerged. Store the vial in upright position.

- Label the 2 ml cryovials with the repository bar codes and remove any institutional identifiers prior to the following procedure.
- Add either formalin or RNALater to the cryovials (be sure to leave room at the top to allow for freezing expansion)
- Place the liver tissue into cryovial.
- Keep Formalin vials at ROOM TEMPERATURE-do not refrigerate or freeze
- Place RNALater vials into -70°C freezer immediately (may be stored in a refrigerator for up to 5 days if freezer access is delayed) until shipment to central repository.
- Update BioDBx with dates of each sample obtained and bar code labels used.
- Frozen liver tissue can be sent with batch shipments of serum. Liver tissue in Formalin must be sent separately at room temperature-DO NOT send with frozen tissue/serum samples.

Transplantation: There are three intraoperative biopsy samples for LDLT and only two (steps #2 and #3) for DDLT

- 1) Donation surgery obtain Tru-Cut needle liver biopsy of right segment along line of resection prior to parenchymal dissection
- 2) Back table: obtain Tru-Cut needle biopsy of donated segment
- 3) 30-60 minutes post-reperfusion: obtain Tru-Cut needle biopsy

Post-transplantation: For HCV positive recipients at the time of protocol biopsies-a percutaneous biopsy tissue core should be obtained. Protocol biopsies are scheduled post-transplant months 3, 12, 24 and 36. Each core should be divided into three equal pieces and packaged as above.

During a liver biopsy for rejection, extra biopsy material will be collected when possible. Based on availability after samples needed for clinical diagnosis, a Tru-Cut needle sample may be obtained and divided into three equal pieces and stored as noted above.

6. Specimen handling

Local arrangements for the specimen collection from the operating rooms will apply. It is essential that the specimens are handled immediately—FASTER is better. The presence of a study coordinator in the operating room at the time of transplant surgery may expedite both the labeling of the specimen.

- All labels are provided by the DCC for each study subject. Keep the individual subject labels separate.
- Specimens are to be inserted in labeled vials.
- Please use the label that is appropriate for the sample.
- Wrap the label lengthwise along the vial.
- Remove all other subject identifiers from the vial.
- Update BioDBx as soon as samples are obtained with date of sample.
- All specimens should be sent to the repository with the monthly shipment.

7. Labels Provided for each subject

Whole blood for **Rutgers** repository (enrollment only)

Serum from the recipient

Serum from donor

Liver Biopsy Tissue Core Samples

7.1 Completing the Shipping Manifest Form

Fill in the header information on the form: (Some of the header information may be preprinted on the form).

- Site and Subject ID: The site id is the three digit number assigned on page 2 above (e.g. Columbia 310). The subject ID is the BioDBx subject number
- Initials of the research staff member who is sending the form and specimen to the repository. Use initials as they appear on the site signature log.
- Date that the sample was collected from the subject (not the date of shipping)
- Date of shipment. Date shipped to repository
- FedEx tracking number from the FedEx airbill.

7.2 BioDBx Sample Tracking – Detailed information

Cohort Study BioDBx Sample Handling Documentation

1. Preparation for subject visit
 - a. Locate the pre-printed labels that the DCC sent to your site. Choose the batch of labels that correspond to the subject's BioDBx number. Put those labels in a location where you can access them for the rest of the study.
 - b. Once you know the date the next visit is scheduled, declare the visit for subject. **YOU MUST DECLARE THE VISIT OR NONE OF THE SUBJECT AND SAMPLE REPORTS WILL WORK PROPERLY!**

- i. Scroll down on the PHI page to the “Contact” window.

Enroll New Subject Show All Subjects Search for Subject

Current User: Joe Bonner [Logout]
 Current Study: A2COH
 Current Site: Test
 Study Programs:
 Demo Web Pages

Contact No.	Contact Date	Contact Type	Made By	Comment	Samples	Actions
	10/15/2004	Enrollment	JBONNER		To Samples	Update/Remove Enter Data
		Qtr1			To Samples	Update/Remove Enter Data
		Qtr2			To Samples	Update/Remove Enter Data
		Qtr3			To Samples	Update/Remove Enter Data
		Qtr4			To Samples	Update/Remove Enter Data
		Qtr5			To Samples	Update/Remove Enter Data
		Txp/Dntn Surg			To Samples	Update/Remove Enter Data
		Day 1			To Samples	Update/Remove Enter Data
		Week 1			To Samples	Update/Remove Enter Data

- ii. Find the appropriate contact timepoint and click “Update/Remove”. A dialogue box will pop up enter the date and “contact made by” fields. If you have any comments you’d like to make, enter them in the box.

Update/Remove Contact for A2COH-R1012

Contact Type

Contact Made By

Contact Date *
(format: mm/dd/yyyy)

Comment

Remove

Note: * fields value required.

- iii. Click the “Update/Remove Contact” Button. Your new contact will be updated and the screen will go back to the PHI/Study Enrollment page.
- iv. Repeat the above steps for each patient visit that is scheduled.

- c. You can now choose to enter data for this subject by clicking the “Enter Data” button.
- d. To update other future contacts, you can access the “Update/Remove Contact” menu by searching for the subject and clicking on the “PHI” button.

2. Printing Bar Codes on Paper

- a. Install the font that the DCC sent you.

- i. Drag it from your email to your desktop and open up your Control Panel.
 - ii. Click on Fonts.
 - iii. In the file menu, click on "Install New Font", and point the destination at your desktop where the font is located.
 - iv. Alternatively, you can copy the font to your clipboard by highlighting it, holding your "Control" Key and the "C" key down at the same time.
 - v. Open your Control Panel and Font folder and hold your "Control" key and the "V" key down at the same time. This will paste the font into the proper folder. You may need to ask your IT staff for help if you don't have install privileges on your computer.
- b. You may print an 8.5" X 11" page of bar codes that correspond to the labels for all of the subjects for whom you've declared a visit. These are for use when scanning the actual samples' bar codes into the system isn't convenient or feasible (i.e. the samples are in the clinic area and you are updating sample collection at your computer in your office).
- c. In BioDBx, click on the Sample Tracker program in the Study Programs window on the upper right side of your screen.



- d. Choose your site.
- e. Click on the folder that says "This Week"
- f. Click on Pending Samples
- g. Scroll Down
- h. Click on Print This Report
- i. Note that the report is by Site. So, you will be viewing all samples that you are expecting to collect from visits you have declared. This may involve multiple subjects and time points.
- j. You can use this reporting feature to look at what samples you have collected and shipped during a current or past week.
- k. You can also see what samples have been received by choosing that report. There will be a delay in seeing what is received since the repository only reports this information to the DCC every two weeks.

Please Choose a site

- Sample Processing Report for A2COH (T) 02-Feb-2005 15:46:08
 - This Week (30-Jan-2005 - 05-Feb-2005)
 - Samples: COLLECTED
 - Samples: PENDING
 - Samples: RECEIVED
 - Samples: SHIPPED
 - Past Weeks
 - Future Weeks

A2COH Sample Processing Report for Northwestern 02

Samples: PENDING for the week beginning 30-Jan-2005

Report run on 02-Feb-2005 15:46:35

Subject	Sample	Status	Type	Date	Contact
R1106	PENDING	Serum Aliquot	Enrollment	->	McKesson



3. Collecting Samples

- Collect the appropriate samples from the patient for that time point, and if necessary, aliquot and place in the appropriate labeled storage vials.
- There is a unique value for each planned sample that goes to McKesson. The 3 tubes of blood for the Genetics Repository all have the same Sample ID.
- Click the link to the Sample Processor in the Study Programs area of BioDBx:

Current User: Joe Bonner [Logout]
Current Study: A2COH
Current Site:
Study Programs:
Demo Web Pages:

In the "Action" box, choose "Log Samples", then click the "Continue" button

Site: Test <input type="button" value="Continue"/>	Action: Log Samples <input type="button" value="Continue"/>
--	---

- d. Scan the bar code for the first sample. Hit the "Tab" key
- e. The fields (other than the date) will prepopulate. Click the "Insert" button. On the lower left, you will see a "Success" message that tells you that you have successfully entered that sample. If you are scanning samples the same day they are drawn then you can leave the date blank today's date will be automatically entered. If you are scanning a date in the past then enter that date information in the "Collected On" box.

Site: Test <input type="button" value="Continue"/>	Action: Log Samples <input type="button" value="Continue"/>
--	---

Sample ID	Collected On	Site Label	Subject Label	Sample Label	
18918	09/23/2004	T	T1130	Aliquot - 1	Seru
18919	09/23/2004	T	T1130	Aliquot - 2	Seru
18916	09/23/2004	T	T1130		Who

Success

- f. Continue scanning and entering samples (for all patients) until you have entered all of the samples you have collected. When you are done inserting the last sample (make sure you click "Insert" for that last sample), Click the "Log Samples" button. You will see a confirmation screen telling you that the samples' status has changed from "Pending" to "Collected"

Site: Test <input type="button" value="Continue"/>	Action: Log Samples <input type="button" value="Continue"/>
--	---

Your Samples have been added to the Log and their status has been updated to Collected

[Click Here To Return Home](#)

- g. The sample's status will change in the subject's information panel as well. You can confirm this by searching for the subject and clicking the blue "samples" button.

Enroll New Subject Show All Subjects Search for Subject

Current User: Steve Middlekauff [Logout]
 Current Study: A2COH
 Current Site: Test
 Demo Web Pages

Current Subject: T1136

[View Subject Samples](#) | [Update Samples](#) | [Add Samples](#) | [Samples Report](#) | [Mole Query](#) | [To Lots](#) | [Storage Units](#)

Brief View Lists View Lots & Lists View

Sample Type	Date Received	Sample Label	Sample Status	Quantity	
Serum (18948)		Aliquot - 1	COLLECTED	1	Sample Record Print Barcode Child Samples (0)
Serum (18949)		Aliquot - 2	COLLECTED	1	Sample Record Print Barcode Child Samples (0)
Whole Blood (18946)			COLLECTED	2	Sample Record Print Barcode Child Samples (0)

4. Preparing samples for shipment

- a. Click the link to the Sample Processor in the Study Programs area of BioDBx:

Enroll New Subject Show All Subjects Search for Subject

Current User: Joe Bonner [Logout]
 Current Study: A2COH
 Current Site: Test
 Study Programs: [Sample Processor](#)
 Demo Web Pages

- b. Choose "Prepare Shipment" action. Click "Continue"

Site: Test Continue	Action: Prepare Shipment Continue	
------------------------	--------------------------------------	--

- c. Choose To Rutgers or To McKesson or To McKesson Cold. Click "Continue"

Site: Test Continue	Action: Prepare Shipment Continue	Select Action: To McKesson Continue
------------------------	--------------------------------------	--

- d. A list of collected samples available to ship to the selected repository will appear. Verify that samples listed are the samples you are ready to ship.
 - i. To remove from list samples that are not ready to be shipped, check the box next to the sample and click "Delete". Those samples will be deleted from that list and their status will be retained as "collected".

Site:

	Sample ID	Collected On	Site Label	Subject Label	Sample Label
<input type="checkbox"/>	18908	09/03/2004	T	T1128	Aliquot - 1
<input type="checkbox"/>	18909	09/03/2004	T	T1128	Aliquot - 2
<input type="checkbox"/>	18913	09/03/2004	T	T1129	Aliquot - 1
<input type="checkbox"/>	18914	09/03/2004	T	T1129	Aliquot - 2
<input type="checkbox"/>	18918	09/23/2004	T	T1130	Aliquot - 1
<input type="checkbox"/>	18919	09/23/2004	T	T1130	Aliquot - 2

- e. When the list is accurate, Print Manifest report by clicking "Print".
- f. Press "Ship" button **Have your Fed-EX shipping bill filled out**
 - i. Enter FedEx shipment number

Explorer User Prompt

Script Prompt:
Enter FedEx Tracking Number

	Sample ID	Collected On	Site Label	Subject Label	Sample Label
<input type="checkbox"/>	18908	09/03/2004	T	T1128	Aliquot - 1
<input type="checkbox"/>	18909	09/03/2004	T	T1128	Aliquot - 2
<input type="checkbox"/>	18913	09/03/2004	T	T1129	Aliquot - 1
<input type="checkbox"/>	18914	09/03/2004	T	T1129	Aliquot - 2
<input type="checkbox"/>	18918	09/23/2004	T	T1130	Aliquot - 1
<input type="checkbox"/>	18919	09/23/2004	T	T1130	Aliquot - 2

- g. Click "OK". A confirmation screen will appear telling you that your samples' status has been changed in the system from "collected" to "shipped". An email will be sent to the DCC and the Repository that has a link to the shipping manifest and tracking number.

Site:

PEGHC@umich.edu, darnms@umich.edu, jbonner@med.umich.edu

Samples marked as Shipped!

[Click Here To Return Home](#)

- h. When you click on the “Samples” button for that subjects’ ID, you’ll see that the status has changed to “Shipped”

Current User: Steve Middlekauff [Logout]
Current Study: A2COH
Current Site:
[Demo Web Pages](#)

Current Subject: [T1130](#)

[View Subject Samples](#) | [Update Samples](#) | [Add Samples](#) | [Samples Report](#) | [Mole Query](#) | [To Lots](#) | [Storage Units](#)

Sample Type	Date Received	Sample Label	Sample Status	Quantity	
Serum (18918)		Aliquot - 1	SHIPPED	1	Sample Record Print Barcode Child Samples (0)
Serum (18919)		Aliquot - 2	SHIPPED	1	Sample Record Print Barcode Child Samples (0)
Whole Blood (18916)			COLLECTED	2	Sample Record Print Barcode Child Samples (0)

5. Other Reporting Functionality

- a. In addition to viewing sample status at a site-specific level, as described above, you can also view sample and form status on a subject level.
- b. Click on the “Subject Status Report” in the drop-down box next to the subject’s PHI button

Current User: Peg Hill-Callahan [Logout]
Current Study: A2COH
Current Site:
Study Programs:
[Demo Web Pages](#)

Label	Last Name	First Name	Med. Rec. No.	Samples	Enter Data	View Data	Discrepancies	Edit Data	View PHI	
R1106				<input type="text" value="247"/>	<input type="text" value="128"/>	<input type="text" value="2"/>		<input type="text" value="2"/>	<input type="text" value="PHI"/>	<input type="text" value=""/>

[Subject Status Report](#)

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- c. A new window will open up showing you the subject's site and ID number with a series of folders and associated dates. Click on the "+" next to the time point for which you want to review the status of forms and samples.



- d. Open the Forms or Samples folder and you can see the status of the pertinent items. Forms are shown as either NotEntered or ENTERED. Sample status is either: Pending, Collected, Shipped or Received:



8. Shipping instructions to the NIDDK Biosample repository (not for whole blood)

Shipment Schedule

Chicago/New York	→	First Monday of each month
Denver/Philadelphia	→	Second Monday of each month
Virginias/UNC	→	Third Monday of each month
San Francisco/Los Angeles	→	Fourth Monday of each month

Frozen sera and liver tissue will be batch shipped to the NIDDK Biosample Repository every month. All shipments should be sent on Monday or the first workday of the week. The repository will supply shipping labels, cryovial boxes, and boxes for shipment. The DCC will supply the cryo vials and barcode labels for the vials.

Exception: Whole blood for cell lines will be shipped immediately to the Rutgers University facility (Genetics Repository).

When ready to ship frozen storage vials, place the vials in a cryo tube box. Each cryo tube box can hold up to 81 (100) samples. All specimens should have been labeled with the pre-printed barcode and all institutional identifiers removed. A shipping manifest form should be printed that lists each sample being shipped.

Make a copy of the manifest: one copy should be sent with the specimens and the other copy should be placed in the subject's research folder.

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Follow all instructions that you receive from the NIDDK repository. Assemble the Medium Dry Ice Shipper according to those instructions. Note the following steps that are described:

1. Place the specimen (cryovial) box and the absorbent strip inside the inner leak proof poly (plastic) bag. (Only one box in each poly bag.)
2. Place the poly bag inside the Tyvek envelope; remove the cover over the adhesive; and seal the flap,
3. Stack up to 4 Tyvek envelopes in the middle of the Styrofoam cooler.
4. Fill the remainder of the space with dry ice.
5. Put the lid on the cooler and place one copy of each shipping manifest (there will be several manifest for each shipment) on top of the cooler lid.
6. Close and tape the outer cardboard box.
7. Stick the label 'Diagnostic Specimens' and a separate address label on the top of the box in the upper right corner.
8. Stick the dry ice label on the top of the box in the upper left hand corner. Enter the weight of the dry ice as 4 kg.
9. Use the pre-printed Fed Ex air bill to ship the specimens to the McKesson/NIDDK Biosample Repository. Fill in Section 1, leaving the "Sender's Fed Ex account number" blank. In Section 7 enter the total weight of the package and a declared value if it is greater than \$100. Place the airbill in the document pouch; remove the larger/lower section of backing and attach it to the TOP of the box. Do NOT seal the pouch.
10. Call Federal Express at 1-800-GO-FEDEX. Give the account number shown in Section 7, Payment, of the pre-printed FedEx Air Bill. FedEx will dispatch a courier to pick up the package.

The address for shipments is:

Rich Frome
McKesson Bioservices
628 Lofstrano Lane
Rockville, MD 20850

All shipments will be sent frozen. Add enough dry ice to ensure shipment will stay frozen overnight (Max wt is 5 lbs). Check to ensure that the box is properly labeled and package according to the shipping policy (see shipping guidelines).

BioDBx will automatically send a message to the DCC and the repository when shipments are sent.

9. NIDDK Repository – Specimen Tracking

Specimen Arrival:

Once specimens have arrived at the Biosample Repository, they will immediately be scanned into the database and the repository will send a notice to the site confirming arrival. As they are logged into the database they will be checked against the shipping manifest. Any discrepancies will be reported

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back to the originating site for verification. After verification and scanning of the samples, they will be placed into -70°C freezers for storage.

10. Bar Coding

Each sample will be assigned a unique barcode. When the sample is received by the repository, its barcode will be scanned and the database will be updated with the date of receipt and its location in the repository. When the sample is shipped from the repository for analysis, the database will be updated with the date of shipment and the destination.

11. Ordering supplies

11.1 Rutgers Cell & DNA Repository

Notify Emily Gymnich or Jacqueline Sabb that additional kits are necessary. This can be done by email (gymnich@biology.rutgers.edu; sabb@biology.rutgers.edu); fax (1-732-445-1149), or phone (1-732-445-1498). Please include the name of the project (A2ALL) and your NIDDK three-digit site number in all communications.

11.2 McKesson Biosciences Repository

McKesson will provide one shipping container at a time. Up to 3 boxes of vials can be shipped within the container. If additional containers are needed, notify Rich Frome, the PI, via email (Rich.Frome@McKessonBio.com), or Heather Higgins, Assistant PI, at NIDDKrepository@mckessonbio.com or call her mobile phone, 240.793.0353. The repository will be moving shortly and other phone numbers will change. The new phone numbers will be provided when available.

11.3 Vials and vacutainers for blood specimens for McKesson repository

The DCC will provide each site with:

- 2 ml vials for the aliquots
- Bar coded labels for the vials

Please contact the DCC by email (A2ALL-staff@umich.edu) to request additional vials or barcode labels. Include in your request the type and amount of vials/labels that you need. Please allow 2-3 weeks time for shipping; do not wait until your supplies are empty before placing your order.

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APPENDIX

Phlebotomy Form – For Rutgers

Flow sheet for blood sample collection -- For Rutgers

Assembly instructions for international Polyfoam mailers -- For the Bioscience Repository

Assembly instructions for one Polyfoam packer – For Rutgers.

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NIDDK GENETICS INITIATIVE

PHLEBOTOMY FORM-A2ALL

SHIP AT ROOM TEMPERATURE IN SAFETY MAILER & ENCLOSE A COPY OF THIS FORM WITH BLOOD KIT

TO: DR. DOUGLAS FUGMAN/GENETICS RUTGERS UNIV./CELL & DNA REPOSITORY DIV. LIFE SCIENCES – NELSON LABS 604 ALLISON ROAD (RM. C120A) PISCATAWAY, NJ 08854-8082	FAX: (732) 445-1149	CHECK _____	FOR RU LAB USE ONLY:
	PHONE: (732) 445-1498	_____	INITIAL: _____
			YELLOW (ACD) ML: _____
			PURPLE (EDTA) ML: _____
			ID#: _____

FROM (NIDDK SITE): **SITE NUMBER** **NUMBER OF TUBES INCLUDED :**

YELLOW (ACD) TOP TUBES: _____ (PED) _____ (ADULT)
PURPLE (EDTA) TOP TUBES: _____ (PED) _____ (ADULT)

NIDDK-A2ALL STAFF: PLACE TUBE LABEL HERE OR COMPLETE BY HAND
(VERIFY INFO AGAINST INFO ON BLOOD TUBES!!!)

SERVICES
CHECK ALL THAT APPLY

AGE: _____ SEX: M _____ F _____

ALTERNATE ID#: **SUBJECT NUMBER**

NIDDK-ID#: **SITE NUMBER-SUBJECT NUMBER**

CELL LINE

BUFFY COAT (PBMC) _____

DNA _____

PLASMA _____

To Be Completed at Collection Site:

DATE BLOOD DRAWN: _____ - _____ - _____ TIME DRAWN: _____ DRAWN BY: _____
MONTH – DAY – YEAR 24 HOURS

CONTACT THE RUTGERS CELL & DNA REPOSITORY TO CONVEY PACKAGE TRACKING NO./DATE OF SHIPMENT (SEE BELOW). IF BLOOD IS SHIPPED ON A FRIDAY FOR SATURDAY DELIVERY, NOTIFY RUTGERS AND CHECK FedEx FORM FOR SATURDAY DELIVERY.

EMAILED/FAXED/

CALL IN TO: _____ RUTGERS UNIVERSITY CELL & DNA REPOSITORY _____/_____/_____
(SEE RUTGERS FAX/PHONE #S ABOVE) DATE TIME (24 HOURS)

PACKAGE TRACKING #: _____ (CHECK SATURDAY DELIVERY ON DELIVERY FORM IF APPLICABLE)

To Be Completed by Rutgers University Cell & DNA Repository

PRIOR NOTIFICATION REC'D: YES _____ NO _____ - IF YES, DATE/TIME _____/_____/_____ AM/PM

CONFIRMATION OF RECEIPT OF BLOOD SAMPLE TO NIDDK SITE SENT BY: _____ DATE _____/_____/_____

**A2ALL STUDY
FLOW SHEET FOR BLOOD SAMPLE COLLECTION
FOR NIDDK GENETICS INITIATIVE AT RUTGERS UNIVERSITY**

- 1) Complete and attach bar code labels to the tubes. **DO NOT write the patient's name or any other personal identification information (e.g. SS#, DOB) on the tubes.**
- 2) Collect blood specimen in the appropriate tubes: three 8.5ml ACD (yellow top) tubes for each recipient or donor. **Be sure to invert each tube gently 6 times to mix blood with additives and keep them at room temperature.**
- 3) Double check NIDDK ID #, verify that ID information on tube matches that on the enclosed NIDDK Phlebotomy Collection Form.
- 4) Check services required for blood sample. Date and sign the NIDDK Phlebotomy Collection Form in the TO BE COMPLETED AT COLLECTION SITE section.
- 5) Package the blood tubes in the safety mailer following the enclosed instructions. Be sure to seal the Styrofoam container with the red tape (water resistant).
- 6) Place the collection form (NIDDK Phlebotomy Collection Form) in the mailer box outside of the plastic bag. Tape cardboard box closed when assembly is complete.
- 7) Use the enclosed Fed Ex shipping label to ship the sample to the Rutgers University Cell Repository. Be sure shipping label is marked for priority overnight delivery.
- 8) For routine shipments be sure the outside of the box is labeled "Diagnostic Specimen Packed in Compliance with IATA Packing Instruction 650."
- 9) **Call Federal Express, 1-800-GO-FEDEX (1-800-463-3339), and a courier will be dispatched to pick up the samples. Be sure to give Fed Ex the Zip Code of the PICKUP address, not that of the destination.**
- 10) **Notify Emily Gymnich and Jacqueline Sabb at the Rutgers University Cell and DNA Repository that blood is being shipped and provide the Federal Express tracking number _____ and NIDDK ID # _____. This can be done by email (gymnich@biology.rutgers.edu; sabb@biology.rutgers.edu), fax (1-732-445-1149), or phone (1-732-445-1498). THIS IS DONE AUTOMATICALLY BY BioDBx**

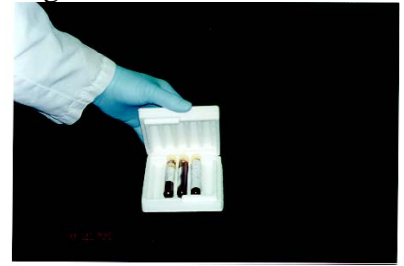
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ASSEMBLY INSTRUCTIONS FOR INTERNATIONAL POLYFOAM MAILERS

READ ALL INSTRUCTIONS THOROUGHLY BEFORE STARTING ASSEMBLY

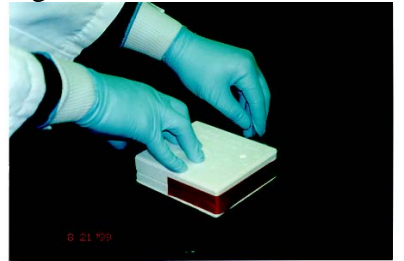
- 1) Place the labeled tubes into the small Styrofoam insert using the same insert that the empty tubes came in (Fig. 1). DO NOT tape the top of the blood tubes.

Fig. 1



- 2) Tape the small Styrofoam insert closed. Peel the backing from one piece of red waterproof tape and begin sealing the Styrofoam lid to the body. Then peel the backing from the second piece of tape and continue sealing the insert, overlapping the first piece of tape about two inches on both ends (Fig. 2).

Fig. 2



- 3) Place the small Styrofoam insert into the press-lock plastic bag. Seal the bag and place it into the large Styrofoam mailer (Fig. 3). Fill the mailer with packing material to prevent disturbing the blood tubes during shipment. Include a copy of the completed Data Collection Form inside the large Styrofoam mailer.

Fig. 3



- 4) Tape the large Styrofoam mailer closed. Peel the backing from one piece of red waterproof tape and begin sealing the Styrofoam lid to the body. Then peel the backing from the second piece of tape and continue sealing the mailer, overlapping the first piece of tape about two inches on both ends (Fig. 4).

Fig. 4



- 5) Slide the Styrofoam mailer into the corrugated carton (Fig. 5) and seal the carton with packing tape. Place the Federal Express International shipping form and any other necessary documents (i.e. International Invoice Form and Declaration Statement on Rutgers letterhead) on the outside of the carton and contact Federal Express FOR PICKUP.

Fig. 5

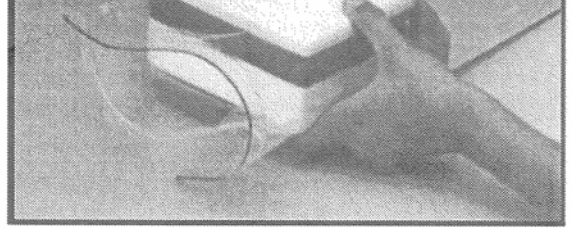


6) Slide the Safety Mailer and open press-lock bag into the corrugated carton (Fig. 4). Then seal the press-lock bag, close the carton using the locking tabs, and place sealing tape (not included) over them.

POLYFOAM Packers

Division of Tuscarora Incorporated
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THE STATE UNIVERSITY OF NEW JERSEY

RUTGERS

Department of Genetics - Cell & DNA Repository

Nelson Biological Laboratories - Room C 120A
604 Allison Road • Piscataway • New Jersey 08854-8082
Phone: 732-445-1498 Fax: 732-445-1149

DECLARATION STATEMENT

The contents of this package are as follows:

- Human whole blood specimens in sealed Vacutainer collection tubes.
- These human blood samples have not been exposed to any animal derived materials such as products derived from livestock or avian disease agents.
- This material is not of tissue culture origin.
- These blood samples are not known to be infectious or contagious.
- **Diagnostic specimens packed in compliance with packing instruction 650.**

These samples are being shipped to the Rutgers University Cell Repository for investigational purposes funded under the National Institute of Diabetes and Digestive and Kidney Diseases Genetics Repository (Contract #N01-DK-3-2610). Samples are packed in approved blood mailers and are perishable. Subjects are being collected for genetic analysis and are not known to be infectious. **Please do not delay.**

These samples are for investigational purposes only and are not required to be screened for HIV or Hepatitis B or C.

If you have any questions or concerns, please contact Dr. Douglas Fugman.

Sincerely,

Dr. Douglas A. Fugman, Ph.D.
Managing Director
Rutgers University Cell & DNA Repository
Phone: 732-445-7024; 732-445-1498
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A. Product Description

RNAlater® is an aqueous, non-toxic tissue storage reagent that rapidly permeates tissue to stabilize and protect cellular RNA in situ in *unfrozen* specimens. Tissue pieces are harvested and immediately submerged in RNAlater for storage without jeopardizing the quality or quantity of RNA. RNAlater eliminates the need to immediately process tissue specimens or to freeze samples in liquid nitrogen for later processing. The figures below show 2 common experiments using RNA isolated from RNAlater-preserved samples.

RNAlater preserves RNA in tissues for up to 1 day at 37°C, 1 week at 25°C, and 1 month or more at 4°C. Tissues can also be stored at -20°C or at -80°C long-term.

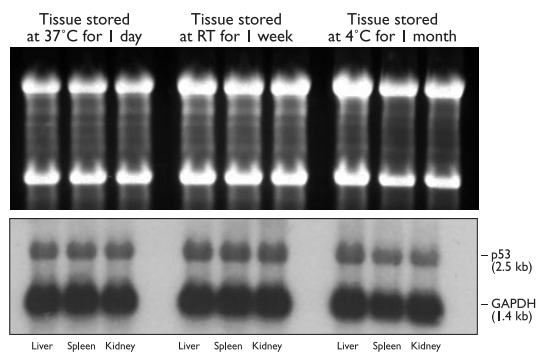


Figure 1. RNA from Tissue Stored in RNAlater

RNA was extracted from mouse tissues stored in RNAlater as shown. The top panel is an ethidium bromide-stained denaturing agarose gel; the bottom panel shows a Northern blot.

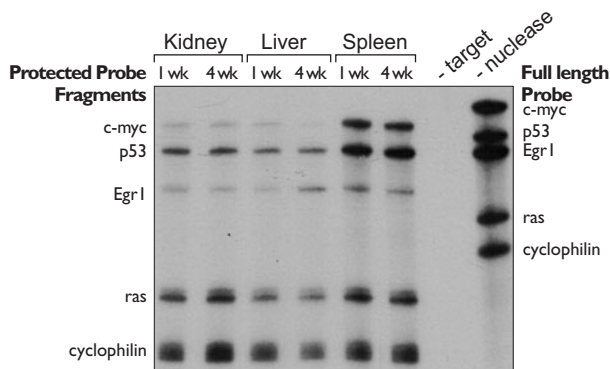


Figure 2. mRNA profiles of mouse tissues stored in RNAlater

The indicated mouse tissues were stored in RNAlater for 1 or 4 weeks at 4°C. RNA was isolated from each tissue and analysed using Ambion's RPA III™ kit. 10 µg of RNA was hybridized with a mixture of 5x10⁴ cpm of each of 5 antisense probes. The gel was exposed to film for 4 hours at -80°C with an intensifying screen.

Storage and Stability

Store RNAlater at room temperature. It is guaranteed for 6 months from the date received.

If any precipitation of RNAlater is seen, heat the solution to 37°C and agitate to redissolve it.

What materials have been tested in RNAlater?

RNAlater has been extensively tested on tissues from several vertebrate species. These include brain, heart, kidney, spleen, liver, testis, skeletal muscle, fat, lung and thymus. RNAlater is also effective for *E. Coli*, *Drosophila*, tissue culture cells, white blood cells, and some plants.

Will RNAlater work with my RNA Isolation Kit?

RNAlater is compatible with most RNA isolation methods. Specifically, we have used RNAlater-preserved samples with TRI Reagent®1, and all of Ambion's RNA isolation kits and reagents, including: RNAwiz™ (one-step disruption/separation reagent), ToTALLY RNA™ (guanidinium isothiocyanate disruption, acid phenol extraction), RNAqueous™ (phenol-free, glass fiber filter binding), PARIS™ (Protein and RNA Isolation System), mirVana™ miRNA Isolation Kit (glass fiber filter microRNA isolation), and MicroPoly(A)Pure™ (direct isolation of poly(A) RNA from guanidinium lysate).

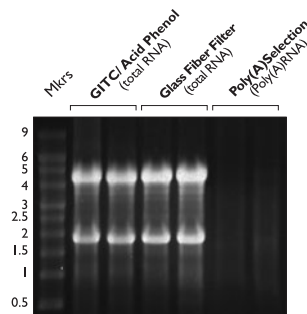


Figure 3. RNA isolated from tissue stored in RNAlater using different isolation methods

Whole mouse hearts and livers were dissected, and placed in RNAlater, in which they were stored for 3 days at 4°C. RNA was isolated from equal mass amounts of each tissue using the indicated Ambion kits. RNA (5 µg) was run on denaturing agarose, stained with ethidium bromide.

Can genomic DNA be obtained from RNAlater-stored samples?

Yes, contact Technical Service and request a protocol.

Can protein be obtained from RNAlater-stored samples?

Yes, proteins are also preserved in RNAlater. Storage in RNAlater will denature proteins, therefore total protein obtained from samples stored in RNAlater will be competent for applications such as Western blotting or 2D gel electrophoresis, but will not be suitable for applications that require native protein.

B. How to use RNAlater

Use RNAlater with fresh tissue only, do not freeze tissue before immersion in RNAlater. Simply cut tissue samples to a maximum thickness of 0.5 cm in any 1 dimension, as long as samples are ≤0.5 cm thick, their size of the other dimensions is not important. Place the fresh tissue in 5 volumes of RNAlater, and store as indicated for the desired temperature.

**NOTE**

Ambion offers RNAlater®-ICE (Cat #7030) as a salvage pathway to recover tissues that have already been frozen. RNAlater-ICE renders frozen tissues pliant enough for homogenization while maintaining low temperatures to protect the RNA from degradation.

1 TRI Reagent, and TRIzol are registered trademarks of Molecular Research Center Inc.

Animal Tissue	RNAlater does not dissolve or disrupt the structure of tissue samples, thus tissue that has been equilibrated in RNAlater can be removed from the solution, sectioned into smaller pieces, and returned to RNAlater if desired. Small organs such as rat liver, kidney and spleen can be stored in RNAlater whole.
Plant Tissue	Many plant tissues can be simply submerged in 5 volumes of RNAlater for storage. We have successfully isolated intact RNA from tobacco leaf explants, entire arabidopsis and alfalfa seedlings, and from potato shoot tips. Plant tissues that have natural barriers to diffusion such as waxy coatings on leaves will probably require disruption to allow RNAlater access to the tissue.
Tissue Culture Cells	Pellet cells according to the protocol followed by your laboratory. Wash to remove the culture medium (e.g. with PBS). Resuspend the cells in a small volume of PBS, then add 5 to 10 volumes RNAlater.
Blood and Plasma	White blood cells can be effectively preserved in RNAlater when separated from the red blood cells and sera and treated as tissue culture cells. RNAlater will preserve RNA in anticoagulated whole blood, sera, and plasma; however, it may be difficult to recover cells or viral particles by centrifugation due to the density of RNAlater. See the RiboPure™ Blood Kit (Ambion Cat #1928) manual for specific instructions on use of RNAlater with whole blood.
Bacteria	RNAlater is bacteriostatic; although bacteria do not grow in RNAlater, the cells remain intact. <i>E. coli</i> stored in RNAlater for 1 month at 4°C are intact and yield undegraded RNA.

C. Storage of Samples in RNAlater

Storage at -80°C

Recommended for archival storage. Incubate samples at 4°C overnight, then remove them from RNAlater before storage at -80°C. For tissue culture cells, do not remove the RNAlater, simply freeze the whole solution. The cell types we have tested do not lyse when frozen at -80°C in RNAlater. Samples can subsequently be thawed at room temperature and refrozen without affecting the amount or the integrity of the recoverable RNA.

Storage at -20°C

Recommended for archival storage. Incubate samples at 4°C overnight, then transfer to -20°C. Samples will not freeze at -20°C, but crystals may form in the storage buffer; this will not affect subsequent RNA isolation. Samples can subsequently be thawed at room temperature and refrozen without affecting the amount or the integrity of the recoverable RNA.

Storage at 4°C

Ambion sees no evidence of RNA degradation in samples stored at 4°C for up to 1 month.

If Refrigeration is not Possible:

Place the samples in as cool an environment as possible. If ambient temperature is above 25°C, incubate samples in RNAlater on ice for a few hours if possible before storing at ambient temperature.

Storage at 25°C

RNA isolated from samples stored at 25°C for one week is intact. In our experience, RNA from samples stored at 25°C for two weeks appears slightly degraded (marginally acceptable for northern analysis, but still of sufficient quality for nuclease protection assay or RT-PCR analysis).

Storage at 37°C

RNA isolated from samples stored at 37°C is intact after a 24 hour incubation, but is partially degraded after a 3 day incubation.

D. RNA Isolation from Material in RNAlater

1. Removing Samples from RNAlater

RNAlater can be discarded down the sink with running water.

Tissue

Tissues that have been stored in RNAlater should be removed from the storage solution with sterile forceps, and submerged in RNA isolation lysis solution. Tissue homogenization should be rapid once the tissue is in lysis/denaturation solution.

Cells

There are two options for isolating RNA from cells stored in RNAlater, the RNAlater can be removed, or the RNA can be extracted from the mixture of cells and RNAlater.

- Removal of RNAlater

Our experience is that cells become much less fragile when stored in RNAlater and can be centrifuged at high speed without lysis. We have successfully centrifuged cells at 5000 x g without loss. Since different cells may respond differently to this force, we suggest you try pelleting a non-valuable sample first to confirm that you can recover your cells this way. An alternative is to dilute the RNAlater by 50% immediately before centrifugation with cold PBS (or other buffered solution) in order to reduce the density of the solution.

- RNA extraction from cells in RNAlater

Alternatively, we have used one-step disruption/extraction solutions (e.g. RNAwiz™, and TRI Reagent) to purify RNA from cells that have not been removed from RNAlater. This can be done by adding ten volumes of the one-step solution to the cell mixture, and proceeding normally. When Ambion's RNAwiz™ is used in this way, it may be necessary to dilute the aqueous phase before the RNA precipitation step, see below for more information.

2. Tips for RNA Isolation

Glass fiber-based extraction

Using glass fiber filter-based RNA isolation kits, it may be necessary to use a centrifuge to push lysates through the filter as opposed to using a vacuum manifold.

One-step disruption/extraction solutions

When using one-step RNA isolation products such as TRIzol® (or TRI Reagent) on RNAlater-preserved samples, occasionally the aqueous phase is cloudy. If this occurs, simply continue the procedure, following the manufacturer's instructions. Cloudiness of the aqueous phase does not affect the quantity or quality of the RNA obtained.

With Ambion's RNAwiz™, there may be a problem getting the aqueous phase to mix with isopropanol at the precipitation step because of RNAlater carryover. If this occurs, simply add a mixture of 50% water, 50% isopropanol until the solution becomes clear and the two phases mix. The amount of water/isopropanol required will depend on how much RNAlater was carried over; if the sample was mostly RNAlater, as much as an equal volume may be needed.

E. RNAlater Specifications

Quality Assurance:

RNAlater undergoes quality assurance testing to verify that its composition is invariant from lot to lot.

Safety:

This product is a proprietary solution whose chemical, physical, and toxicological properties have not been thoroughly investigated. See the following MSDS for more information.

F. RNAlater® Material Safety Data Sheet

Physical data

Appearance and odor	clear liquid, slightly viscous
Boiling point	n/a
Solubility in H ₂ O	soluble

Fire and explosion hazard data

Flash point	n/a
Flammable limits in air	n/a
Extinguishing media	water, CO ₂ , foam, dry chemical (Use any means suitable for extinguishing surrounding fire)
Special fire fighting	Wear self-contained breathing apparatus and protective clothing.
Fire/explosion hazards	Irritating and/or toxic gases or fumes may be generated by thermal decomposition or combustion.

Health hazard data

Effects of overexposure	Acute overexposure may cause irritation to eyes, skin, and respiratory tract.
Emergency first aid	Flush affected area with copious amounts of water. Irrigate eyes and skin for ≥15 minutes. Contact physician if irritation occurs due to salt content.

Reactivity data

Stability	stable
Incompatibility	n/a
Haz. Decomp. Products	n/a
Hazardous Polymerization	n/a

Spill or leak procedures

If released or spilled	Ventilate area. Absorb spill with inert material. Place in container with a lid. Wash spill area after cleanup.
Waste disposal method	Dispose of according to federal, local and state regulations.

Special protection and precaution information

Respiratory protection	Not expected to require personal respirator usage. (Use NIOSH approved respirator if necessary)
Ventilation	Not expected to require special ventilation
Precautionary labeling	none
Handling and storage considerations	Laboratory aprons and gloves. Do not store in aluminum or copper containers. Keep tightly closed in a cool, dry place.

This bulletin is for your guidance and is based upon information and tests believed to be reliable. Ambion makes no guarantee of the accuracy or completeness of the data and shall not be liable for any damages thereto. The data are offered solely for your consideration, investigation, and verification. These suggestions should not be confused with either state, municipal, or insurance requirements, or with national safety codes and constitute no warranty. Any use of these data and information must be determined by the user to be in accordance with applicable federal, state, and local regulations.