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Clinical Study RDCRN Protocol 6801

Manual of Procedures

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1. Introduction

1.A. Nephrotic Syndrome Study Network Overview

The Nephrotic Syndrome Rare Diseases Clinical Research Study Network (NEPTUNE) is a landmark research project aimed to establish concerted and innovative investigational strategies combining basic science, translational, and clinical methods to study FSGS, MCD, and MN.

It will focus research activities on the prediction and molecular mechanisms of Focal Segmental Glomerulosclerosis (FSGS), Minimal Change Disease (MCD), and Membranous Nephropathy (MN) as well as developing a robust biological specimen archive for future investigative work on a longitudinally followed cohort of incipient, biopsy-proven diagnoses for these rare diseases.

1.A.1. Objectives

The overarching aim of the Nephrotic Syndrome Study Network is to establish a collaborative resource for nephrology researchers interested in FSGS, MCD, and MN with the following objectives:

1. Establish a collaborative, integrated, and cost-effective investigational infrastructure to conduct clinical and translational research in Focal and Segmental Glomerulosclerosis, Minimal Change Disease, and Membranous Nephropathy;
2. Perform a longitudinal observational cohort study of patients who present with biopsy-proven Focal and Segmental Glomerulosclerosis or Minimal Change Disease;
3. Perform a longitudinal observational cohort study of patients who present with biopsy-proven Membranous Nephropathy;
4. Administer a pilot and ancillary projects program that selects, supports, and coordinates studies that employ the unique resources, clinical data, or specimens assembled by NEPTUNE;
5. Implement a training program designed for advanced post-doctoral and junior faculty trainees, or established investigators interested in redirecting their investigative focus, who are preparing to become independent investigators in clinical and translational research in human glomerular disease;
6. In collaboration with the NIH Rare Disease Clinical Research Network Data Management Coordinating Center (DMCC) and two well-established disease-specific lay foundations (The NephCure Foundation and Halpin Foundation), develop and maintain a web-based platform for the exchange of information for lay people, physicians, and scientists interested in FSGS, MN, or MCD.

1.A.2. Description

At study start, 15 sites have been identified and collectively will enroll two cohorts of participants: 250 for FSGS/MCD, 200 for MN. As of Protocol V3.0, three additional sites have been added and are recruiting (Columbia, Emory, and Temple Universities) with the addition of Stanford University and the University of Illinois at Chicago soon to be activated. This baseline cohort will be followed for up to five years and will include a racially and ethnically diverse group of both adult and pediatric patients, with a biopsy-proven incipient diagnosis of the study diseases. Consented participants who subsequently do not qualify histologically will be maintained as a third study cohort as non-FSGS/MCD/MN participants (Other Glomerulopathies or OG); providing these participants are not later identified to be ineligible post-biopsy due to delayed clinical blood tests identifying exclusion criteria.

1.B. Study Organization

At study initiation, participants will be recruited from the following Clinical Centers and their associated clinical sites as listed below, updated sites can be found at http://rarediseasesnetwork.epi.usf.edu/NEPTUNE/centers/index.htm.

1.B.1. Clinical Centers (CC) and Sites

NAME	LOCATION
Case Western Reserve University MetroHealth Medical Center	Cleveland, Ohio
Columbia University	New York City, New York
Children's Hospital of Los Angeles	Los Angeles, California
Emory University	Atlanta, Georgia
Harbor Medical Center	Torrance, California
Johns Hopkins School of Medicine University of Maryland	Baltimore, Maryland
Cohen Children's Hospital	New Hyde Park, New York
Mayo Clinic	Rochester, Minnesota
Montefiore Medical Center	Bronx, New York
National Institutes of Health National Institute of Digestive, Diabetes & Kidney Diseases, Intramural	Bethesda, Maryland
New York University Medical Center	New York, New York
Stanford University	Stanford, CA
Temple University	Philadelphia, Pennsylvania
University Health Network University of Toronto	Ontario, Canada
University of Illinois at Chicago	Chicago, IL
University of Miami Miller School of Medicine	Miami, Florida
University of Michigan Medical Center	Ann Arbor, Michigan
University of North Carolina at Chapel Hill	Chapel Hill, North Carolina
University of Pennsylvania Children's Hospital of Philadelphia	Philadelphia, Pennsylvania
University of Washington Medical Center	Seattle, Washington

Seattle Children's Hospital
Sacred Heart Medical Center

1.B.2. Participating Laboratories and Reading Centers

CENTRAL SITE	PRINCIPAL INVESTIGATOR
NEPTUNE Biobank	Matthias Kretzler, MD
Urine Proteomics Biobank	Fernando Fervenza, MD, PhD
NIDDK Histopathology Data Archive	Jeffrey Kopp, MD and Stephen Hewitt, MD, PhD
NIDDK Biorepository	Rebekah Rasooly, MD

1.B.3. Data Analysis and Coordinating Center

The University of Michigan will serve as the primary Data Analysis and Coordinating Center (DACC). As a cost-share funded study partially funded through the Office of Rare Diseases Research (ORDR), a Rare Disease Clinical Research Network exists through which limited study data will be deposited and backed up at regular intervals.

1.B.3.a. *Velos eResearch Data Management*

Velos eResearch is a clinical trial data management system (CTMS) that will be used by the NEPTUNE Research Coordinator team to collect, store, and manage data using web-based technology. Velos is a commercially developed, regulatory-compliant, web-based system. System training and access for the NEPTUNE study will be regulated by the NEPTUNE DACC Data Manager.

1.B.3.b. *Velos Training and Certification*

All Training and certification materials are located in Appendix A. System training and access for the NEPTUNE study will be regulated by the NEPTUNE DACC Data Manager.

1.B.3.c. *Local Versus Central Data Entry*

In response to research coordinator study burden concerns, effective Protocol Version 3.0, Central Data Entry is an option for all sites within NEPTUNE. Registration and initial study data must be entered locally to protect the participant's confidentiality.

All sites are responsible for registering their participants into Velos and completing the following Velos documentation and Case Report Forms (CRFs):

i. Date Informed Consent was completed
ii. Relevant data from Informed Consent documented via the unscheduled event action in Velos (see Velos MOP)
iii. Limited data set from the Eligibility Assessment Worksheet (Form 1)
iv. Velos Registration Details (Form 2A)
v. Demographic data required for proper participant enrollment in Velos
vi. Necessary demographic data in the Baseline Participant Information (Form 4A), as these responses are generated from the Eligibility Assessment Worksheet (Form 1)
vii. Kidney Specimens (Form 11A) documentation Parts I-III

1.B.4. Funding

Funding for NEPTUNE is a collaborative public and private effort. In response to RFA-OD-08-001, this network is funded through the National Institute for Diabetes, Digestive and Kidney Diseases (NIDDK), and the Office of Rare Diseases Research (ORDR), both divisions of the National Institutes of Health (NIH) under the Department of Health and Human Services (DHHS), as well as cost-sharing provided by the University of Michigan Medical School (UMMS) and approximately 25% of the overall budget supplemented by a private non-profit organization, The NephCure Foundation, a key organization for fundraising efforts specifically for Nephrotic Syndrome and FSGS.

1.B.5. Project Cycle

This study is currently funded via a mechanism allowing only 1-five year funding period with funding beginning September 8, 2009 and following the budget year cycle for July 1 – June 30.

1.B.6. Sub-Cohort Selection

As ancillary studies are submitted, reviewed, and approved, cohort selection will be determined by the submitting PI and the Steering Committee.

1.C. General Policy

1.C.1. General Protocol Policy

The objectives of the study are most likely to be achieved if the protocol does not require alteration. Any changes in the protocol will result in some degree of heterogeneity of the data, which complicates the analyses and may compromise the scientific integrity of the study. However, occasions may arise in which protocol changes are necessary. Therefore, changes in the protocol will be considered only if they are required to ensure participant safety or will significantly enhance the scientific validity of the study.

The Steering Committee must approve all protocol amendments or revisions. In turn, these amendments and/or revisions will require approval from the RDCRN as well as the NIDDK. Approved amendments must be submitted to the local site IRB's for approval and once approved, be incorporated into the protocol. IRB approval must occur prior to the implementation of an amendment. Amendments that include minor changes to the protocol may undergo expedited review if these changes fit into expedited approval criteria. All changes to the informed consent form must also be approved by the local site IRB.

1.C.2. Human Subjects Considerations

Regulatory Requirements for Informed Consent

Each Clinical Site is responsible for ensuring that informed consent is obtained from each participant using a current consent form according to the guidelines of its local Institutional Review Board (IRB) and in accordance with the Common Rule (45 CFR Part 46 subpart A, Protection of Human Subjects). The informed consent form must be obtained or on file (signed and dated by the participant) prior to initiation of any study related activity.

The Informed Consent form must provide the following information to each participant:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the participant's involvement, a description of the procedures to be followed, and identification of any procedures which are experimental.
- A description of any reasonably foreseeable risks or discomforts to the participant.
- A description of any benefits to the participant or to others which may reasonably be expected from the research.

- A disclosure of appropriate alternative procedures or courses of treatment, if any that might be advantageous to the participant.
- A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained.
- For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and who to contact in the event of a research related injury to the participant.
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

Administration of Informed Consent

Each participant will be asked to sign one or more Informed Consent documents depending on the structure of the document at each Clinical Site to continue to be followed. These documents describe the Nephrotic Syndrome Study Network (NEPTUNE) as well as the genetic sample component of the study. These document(s) contain embedded YES/NO questions with signature requirements. Instruct the participant to read the Informed Consent(s) carefully and to raise any questions or concerns that he/she has and to sign ONLY after their questions or concerns have been answered fully. Participant questions should be answered using lay language.

Participants may decide to participate in the NEPTUNE Study but opt out of all, or parts, of the genetic data collection. Discuss the options and implications of participation in the genetics portion and explain the selections contained in the YES/NO questions about genetic samples. It is highly important to relay to potential participants that our study will be investigating genetics related to kidney disease.

As an added measure of protection, and as required by the Lead Site IRB, Genetic Information Nondiscrimination Act language has been added to the study template as follows:

> A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:
>
> - Health insurance companies and group health plans may not request your genetic information that we get from this research.
> - Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
> - Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when settling the terms of your employment.
>
> All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 more employees must follow this law as of November 21, 2009.
>
> Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Participants are also requested to consent to release their contact information to The NephCure Foundation. An embedded YES/NO question for the potential participants is a part of the informed consent template. Potential participants may continue in the NEPTUNE study without consenting to release their information to NephCure.

Consenting participants have the opportunity to be directly informed of studies for which they may potentially qualify based on their NEPTUNE study data when they consent to this study option.

Participants should be made aware of the possibility their diagnosis will not meet the eligibility criteria and that they may not be able to continue in the study. Participants may opt in/out of maintaining their collected samples as part of the NEPTUNE biorepository.

Provide a copy of the signed form to the participant before they leave the clinical center and instruct the participant that they should feel free to contact the clinical center should further questions occur to them after the visit.

It is possible that informed consents will be revised or amended throughout the course of the study. If so, a revised informed consent must be obtained from participants at follow-up prior to further collection of information or performing study procedures.

1.C.3. Participant Confidentiality

HIPAA

Participants are required to sign a Health Insurance Portability and Accountability Act (HIPAA) Authorization upon enrollment into the study. The HIPAA Authorization may or may not be incorporated into the Nephrotic Syndrome Study Network consent depending on the policy of the Clinical Center. This form describes both the kinds of health information collected in this study and also all of the disclosures of health information that will be made. The form must also list parties to whom disclosures of personal health information will be made.

Sites external to the Unites States must comply with equivalent national standards (Canadian sites are required to utilize the Personal Health Information Protection Act (PHIPA)) upon study enrollment.

Medical Record Release

This study may require the release of medical records from remote health care facilities. Each Clinical Center should obtain written authorization for the release of medical records from each study participant annually. The following procedures are recommended:

- During The Informed Consent/HIPAA Authorization process, each participant will be asked to sign and date three (3) copies of the Medical Release Form. It was communicated that these will be issued as needed to obtain data for the research study. (The release of medical records should be listed in the HIPAA authorization form that they should have previously signed.)
- A copy of the signed release form can be obtained for the Clinical Site's records. Remote institutions may require the form with *original* signatures.
- Intermittently check with your institution to see if the Medical Release Form has been revised.
- Each study participant should sign three (3) currently dated Medical Release Forms during their yearly site visit(s) (Authorization to Request Patient Information, Authorization to Release Information, and each sites local Medical Release Form).

Additional Confidentiality Concerns

- Consent form(s), HIPAA authorizations and source documentation must be securely maintained in a participant research chart.

- Recruited study participants are assigned a Participant Study ID number, a unique study identification number. Creation of a unique Participant Study ID number is outlined in detail in Section 3.D.
- **All communication between the Data Analysis and Coordinating Center (DACC) Principal Investigators, personnel, and staff and the Clinical Centers Site-Investigators, personnel, and staff regarding participant data occurs via the Participant Study ID number only. Clinical Site personnel are responsible for maintaining a key code for all participants, and stored within an appropriate locked file system**.

2. Participant Recruitment

2.A. Recruitment Overview

Clinical centers are committed to recruiting a total of 450 study participants meeting the eligibility requirements for Focal Segmental Glomerulosclerosis and Minimal Change Disease (FSGS/MCD Cohort) and Membranous Nephropathy (MN Cohort).

2.B. Visit Schedule Information

Table 1 below describes the visits used throughout this manual to describe interaction with NEPTUNE participants. The participant study calendar, which is a tool available in Velos eResearch, will be generated based on the date of the Baseline visit [V2]. All contacts and visits will have a permissible window (±30 days) of contact surrounding them that defines the period of time during which a visit is considered on time (i.e., visit window). Every effort should be made to conduct study visits at regular intervals.

Table 1. NEPTUNE Visit Schedule

Pre-Screen	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13
[V0]	[V1]	[V2]	[V3]	[V4]	[V5]	[V6]	[V7]	[V8]	[V9]	[V10]	[V11]	[V12]	[V13]
Chart Review or MD referral	Screen/ Eligibility	Baseline	Biopsy	4 months Follow-up	8 months Follow-up	12 months Follow-up	18 months Follow-up	24 months Follow-up	30 months Follow-up	36 months Follow-up	42 months Follow-up	48 months Follow-up	54-60 months Follow-up

2.C. Cohort Selection

Two prospective cohort studies will be performed, namely: (1) The FSGS/MCD Cohort Study and (2) the MN Cohort Study. Each cohort study is a prospective incident cohort study (n=250 for the FSGS/MCD study and n=200 for the MN study) using a consecutive sampling frame. Each cohort study is population-based, that is, all subjects who meet the inclusion criteria at the participating centers will be enrolled if the subjects or their legal guardians provide comprehensive written informed consent. Each study will be performed simultaneously at the participating clinical centers listed in Section 1.B.1. A recruit-to-replace strategy will be employed throughout the enrollment phase until the end of the funding cycle.

2.C.1. Inclusion Criteria

FSGS/MCD Cohort:

Adult and pediatric participants

A definition for FSGS/MCD will require the documented presence of significant proteinuria (≥ 500 mg/24 hours or spot protein: creatinine ratio ≥ 0.5) within 90 days of the screening date and a pathologic diagnosis as recorded in the biopsy report including one of the following categories:

- Minimal change disease
- Minimal change nephrotic syndrome
- Glomerular minimal changes with nephrotic syndrome
- Extensive foot process effacement suggestive/consistent with minimal change disease or minimal change nephrotic syndrome
- Focal segmental glomerulosclerosis, any variant according to the Columbia classification

- Collapsing glomerulopathy, any etiology
- Tip lesion (not necessarily FSGS variant)
- Diffuse mesangial sclerosis

The histological classification will be reviewed by the pathology committee to verify accuracy (See Appendix B Pathology Manual of Procedures for detailed characterization of FSGS/MCD biopsies).

MN Cohort:

A definition of MN will require the documented presence of significant proteinuria at presentation (≥ 500 mg/24 hours or spot protein: creatinine ratio ≥ 0.5) within 90 days of the screening date and a pathologic diagnosis as recorded in the biopsy report including one of the following categories:

- Membranous glomerulopathy or glomerulonephritis
- Idiopathic membranous glomerulopathy or glomerulonephritis
- Membranous glomerulopathy or glomerulonephritis, consider idiopathic form
- Membranous glomerulopathy or glomerulonephritis, consider secondary form

The histological classification will be reviewed by the pathology committee to verify accuracy (See Appendix B Pathology Manual of Procedures for detailed characterization of MN biopsies).

These diagnostic criteria are based on a uniformly accepted minimum requirement for clinical diagnosis of the respective conditions in North America. As standardized guidelines and findings from new studies become available, it is anticipated that the definitions for these glomerular disorders will evolve and improve, as well as being represented in this manual of procedures accordingly.

Other Glomerulopathies:

Patients initially enrolled in the study who undergo renal biopsy with biospecimen procurement at Visits 2 and 3, and who do not fulfill the histology inclusion criteria of the Nephrotic Syndrome Study Network are potentially candidates for inclusion in separately funded studies. We expect to have identified additional resources by the time enrollment starts to allow us to follow these patients in an independent protocol.

2.C.2. Exclusion Criteria

- Prior solid organ transplant
- A clinical diagnosis of glomerulopathy without diagnostic renal biopsy
- Clinical, serological or histological evidence of systemic lupus erythematosus (SLE) as defined by the ARA criteria. Patients with membranous in combination with SLE will be excluded because this entity is well defined within the International Society of Nephrology/Renal Pathology Society categories of lupus nephritis, and frequently overlaps with other classification categories of SLE nephritis (68)
- Clinical or histological evidence of other renal diseases (Alport, Nail Patella, Diabetic Nephropathy, IgA-nephritis, monoclonal gammopathy (multiple myelomas), genito-urinary malformations with vesico-uretheral reflux or renal dysplasia)
- Known systemic disease diagnosis at time of enrollment with a life expectancy less than 6 months

- Unwillingness or inability to give a comprehensive informed consent
- Unwillingness to comply with study procedures and visit schedule
- Institutionalized individuals (e.g., prisoners)
- Laboratory information unavailable prior to consent and biopsy procedure subsequently supporting exclusion criteria will deem a participant ineligible

2.C.3. Eligibility Verification

Consented individuals determined to be ineligible post-procedure will be requested to consent for their tissue to remain part of the NEPTUNE biorepository. These samples may serve as non-nephrotic control samples for future studies and consenting participants will be compensated up to $50 or as allowed by local IRBs.

2.D. Study ID Numbers

2.D.1. Participant Study ID Number Assignment

Once eligibility has been determined, and the individual has signed the Informed Consent Document, a unique Study ID can be assigned. The Study ID will be assigned by the institution recruiting the participant and will contain the following components:

- Year of Enrollment (10, 11, 12 to indicate 2010, 2011, 2012, respectively)
- Study Number (the Study Number is 26609 and represents the lead site (University of Michigan) IRB Approval number providing study identification to all samples and data)
- Clinical Site ID (designated below in Table 2)
- Participant Number (this is the chronological participant number beginning with 1 and incrementing by 1's with leading zeroes for adult participants; beginning with 501 and incrementing by 1's for pediatric participants. Please note this distinction is strictly for identifying adult versus pediatric specimen kits at sites recruiting for both patient populations).

Table 2. Clinical Site ID's

Participant ID			
Year	StudyID	Site ID	Participant #
10 11 12 13 14	26609	000 = U Michigan 001 = NYUMC 002 = Johns-Hopkins 007 = U Illinois at Chicago 009 = Toronto 096 = Credit Valley 097 = York Central 098 = Sunnybrook 099 = Scarborough 020 = Case Western Res Univ 021 = Children's Hosp - LA 022 = Harbor - UCLA 023 = Long Island Jewish 024 = Mayo 025 = Montefiore	001 002 003 … … … … 011 012 … … … … …

		026 = Univ Miami 027 = Univ N Carolina 028 = U Penn 029 = U Wash 030 = NIDDK 031 = Columbia 032 = Temple 033 = Emory 034 = Drexel **036 = Stanford**	501 502 …

Light text indicates a sub-site of a NEPTUNE Site

Example Participant Study ID:

08-26609-000-001 = **Adult** participant enrolled in **2008** for the **NEPTUNE Study** at the **University of Michigan**, **participant #1**.

08-26609-000-501 = **Pediatric** participant enrolled in **2008** for the **NEPTUNE Study** at the **University of Michigan**, **participant #1**.

The participant's study ID will

2.D.2. Velos Patient ID Number Assignment

Once eligibility has been determined, and the individual has signed the Informed Consent Document, a unique Velos Patient ID can be assigned. The Patient ID is a subset of the Study Participant ID. The Velos Patient ID will be assigned by the institution recruiting the participant and will contain the following components:

- Clinical Site ID (Designated above in Table 2)
- Participant Number (this is the chronological participant number beginning with 1 and incrementing by 1's with leading zeroes for adult participants; beginning with 501 and incrementing by 1's for pediatric participants. Please note this distinction is strictly for identifying adult versus pediatric specimen kits at sites recruiting for both patient populations).

Example Patient Study ID:

000001 = Adult participant enrolled at the **University of Michigan**, **participant #1**.

000501 = Pediatric participant enrolled at the **University of Michigan**, **participant #1**.

3. Pre-Screening/Eligibility [V0]

Each clinical center is committed to recruiting participants based on preliminary review of historical cases identified through the Clinical Center's patient populations.

Specific directions for completing all worksheets referenced in the following sections are found in Appendix C for the NEPTUNE Study Worksheet References.

3.A. Pre-Screening Overview

Potential participants will be identified by reviewing the medical record of subjects being seen in clinic for diagnosis of kidney disease or patients presenting for a diagnostic renal biopsy and recorded in the NEPTUNE screening log. As necessary, a partial waiver of informed consent will be obtained from site specific institutional review boards to screen these potential participants. Once identified by either a RC or a nephrology team member (not limited to site physicians, nurses, clinic staff and study personnel aware of the study), a clinical caregiver will request permission for the approved NEPTUNE team member to approach the potential participant to discuss the NEPTUNE Study (Please see 3.B.1 Obtaining Permission to Approach Potential Participants).

Prior to [V1] (Table 1. pre-screening visit), the RC will complete the first portion of the Eligibility Assessment Worksheet (Form 1). The RC will bring this form with them to the Screening/Eligibility Visit [V1] and complete the remainder of the form with the potential participant if that individual is interested in participating.

3.A.1. Eligibility Assessment Worksheet (Form 1) Part I

- Initials of persons screened (Subject Initials)
- Date of pre-screening (Initial Chart Review / PI Referral date)
- Preliminary Demographic Information including: Gender, Age, Ethnicity, Race (to be confirmed with consented participants)
- Inclusion Criteria Checklist (*all requiring affirmative response)*: Renal Biopsy Scheduled, Documented Urinary Protein Excretion ≥ 500 mg/24 hours or Spot Protein to Creatinine ratio ≥ .5 at the time of diagnosis or within 3 months of the Screening Visit and Documentation by Date and Value
- Exclusion Criteria Checklist (*all requiring negative response)*: Solid Organ Transplant, evidence of SLE, evidence of Alport, nail patella, Diabetic Nephropathy, IgA-Nephritis, monoclonal gammopathy, genito-urinary malformations with vesico-uretheral reflux, or Renal Dysplasia, Systemic Disease with < 6 months life expectancy, currently institutionalized

3.A.2. Screening Log

A log will be kept at each site, in a locked cabinet, not to be distributed, which will contain the following details:

- Initials of persons screened (Subject Initials)
- Date of pre-screening (Initial Chart Review / PI Referral date)
- Gender, Race, Age Group (Over 18?)
- Indication that pre-screening eligibility questionnaire (Form 1, Part I) complete (Eligible Y/N)

- Date of in-person screening Visit 0 (Form 1, Part II)
- Indication that individual signed consent or not (V1, Date Consented)
- If individual not enrolled, brief description of reason
- Signature/Date of RC who screened the individual

This log should be directed to the NEPTUNE DACC on a monthly basis, prior to the monthly Research Coordinator Conference Call or as arranged between the local site and the DACC.

4. Screening Contact [V0]

4.A. Obtaining Permission to Approach Potential Participants

Once an individual has been identified through the pre-screening process, and has been deemed potentially eligible by concurrence of a study team member and physician investigator, they will be approached by a clinical caregiver to request permission for the RC to initiate discussion of the NEPTUNE Study with them.

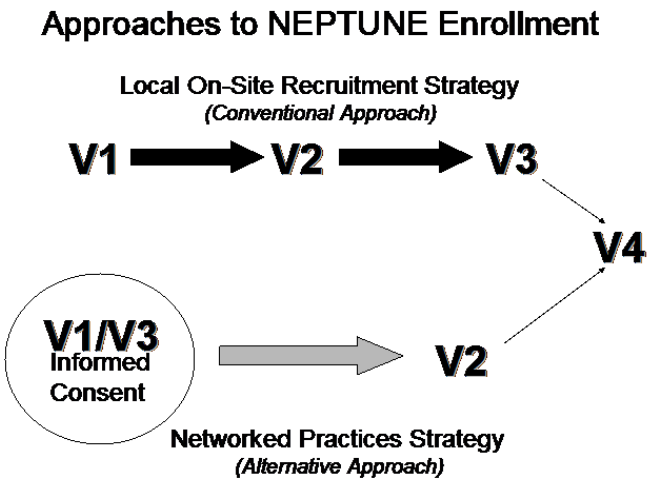
4.B. Visit Overview

This visit serves as an introductory visit for pre-screened individuals who appear to be potential candidates for the NEPTUNE Study. Ideally, this visit will occur at the time of a nephrology clinic visit or consultation. During this visit, eligibility will be reviewed with the potential candidate and the RC will assess level of interest.

All pre-screened individuals who appear to be potential candidates for the NEPTUNE Study should receive the NEPTUNE Registry brochure, as well as The NephCure Foundation brochure (IRB approval required).

Suggested language to approach a potential participant is included in Appendix D.

4.B.1. Approaching Potential Participants



In Clinic (Conventional Approach):

Once approval has been obtained to contact the potential participant, he/she will be approached in the appropriate clinic. A RC will inform the individual of the study and ask if they are willing to hear more about the study (see suggested screening language).

If the Potential Participant Agrees:

1. If, at this point, the individual is interested in learning more about the study, the RC will complete the second half of the Eligibility Assessment Worksheet (Form 1) with the individual.

2. If the individual is eligible based on the completed Eligibility Assessment Worksheet (Form 1), and interested to participate in NEPTUNE, the overall study details will be discussed with them. If time permits the Informed Consent Process (Section 1.C.2 and 1.C.3) should be initiated.

    a. After the informed consent has been reviewed and signed, complete the Velos Enrollment worksheet (Form 2A), assign the participant a study ID number and enroll him/her into the NEPTUNE study.

    b. As time permits, begin the Medication Log, and collect Contact Information, Healthcare Provider Information on the respective worksheets (Forms 2B, 3 and 5). Please note a medication log must be started prior to the biopsy.

    The information in Forms 1, 2A/B, 3 and 5 should then be transferred into the Velos CRFs.

        i. Local data entry: Upon data entry of Forms 1, 2A/B, 3, 4A (Ethnicity and Race information only) and 5 [V1] is now complete.
        ii. Central data entry: Upon completion of Forms 1, 2A/B, 4A (Ethnicity and Race information only) Velos documentation is complete for [V1]. Forms 3 and 5 must be sent to the DACC within 7 days for [V1] completion.

    c. Provide the patient information about the NEPTUNE Registry and The NephCure Foundation and answer any questions they may have about the registry study.

    d. Schedule or complete the limited elements of the Baseline Visit [V2].

3. If the individual is not eligible based on the completed Eligibility Assessment Worksheet (Form 1), thank them for considering the study and for their time.

    a. Provide the patient information about the NEPTUNE Registry and The NephCure Foundation and answer any questions they may have about the registry study.

    b. Provide a brief follow-up so they know they are valued as patients and have a conclusive response from the study.

4. PLEASE REMEMBER TO RECORD THIS INFORMATION ON THE SCREENING LOG AT YOUR SITE.

In the Outpatient Procedures Area (Alternative Approach, Day of Biopsy):

Once approval has been obtained to contact the potential participant, he/she will be approached in the relevant pre-biopsy area. A study team member will inform individual of the study and ask if they are willing to hear more about the study (see suggested screening language).

If the Potential Participant Agrees:

1. If, at this point, the individual is interested in learning more about the study, the RC will complete the second half of the Eligibility Assessment Worksheet (Form 1) with the individual.

2. If the individual is eligible based on the completed Eligibility Assessment Worksheet (Form 1), and interested to participate in NEPTUNE, the overall study details will be discussed with them. The RC will begin the Informed Consent Process (Section 1.C.2 and 1.C.3).

    a. After the informed consent has been reviewed and signed, complete the Velos Enrollment Worksheet (Form 2A), assign the participant a study ID number and enroll him/her into the NEPTUNE study.

b. As time permits, begin the Medication Log, and collect Contact Information, Healthcare Provider Information on the respective worksheets (Forms 2B, 3 and 5). Please note a medication log must be started prior to the biopsy.

The information in Forms 1, 2A/B, 3 and 5 should then be transferred into the Velos CRFs.

iv. Local data entry: Upon data entry of Forms 1, 2A/B, 3, 4A (Ethnicity and Race information only) and 5 [V1] is now complete.
v. Central data entry: Upon completion of Forms 1, 2A/B, 4A (Ethnicity and Race information only) Velos documentation is complete for [V1]. Forms 3 and 5 must be sent to the DACC within 7 days for [V1] completion.

c. Provide the patient information about the NEPTUNE Registry and The NephCure Foundation and answer any questions they may have about the registry study.

d. Schedule or complete the limited elements of the Baseline Visit [V2].

3. If the individual is not eligible based on the completed Eligibility Assessment Worksheet (Form 1), thank them for considering the study and for their time.

a. Provide the patient information about the NEPTUNE Registry and The NephCure Foundation and answer any questions they may have about the registry study.

b. Provide a brief follow-up so they know they are valued as patients and have a conclusive response from the study.

4. PLEASE REMEMBER TO RECORD THIS INFORMATION ON THE SCREENING LOG AT YOUR SITE.

<u>If the Potential Participant is Not Interested or Ineligible:</u>

1. If the potential participant is ineligible or uninterested in the study, thank them for considering the study and for their time.
2. Provide the patient information about the NEPTUNE Registry and answer any questions they may have about the registry study.
3. Provide a brief follow-up so they know they are valued as patients and have a conclusive response from the study.
4. PLEASE REMEMBER TO RECORD THIS INFORMATION ON THE SCREENING LOG AT YOUR SITE.

4.B.2. Eligibility Assessment Worksheet (Form 1) Part II

Prior to [V1] (Table 1. pre-screening visit), the RC will complete the first portion of the Eligibility Assessment Worksheet (Form 1). The RC will bring this form with them to the Screening/Eligibility Visit [V0] and complete the remainder of the form with the potential participant if the individual is interested in learning more about the study.

Information collected from the potential participant in Form 1 Part II includes the following:

- Date of Eligibility Visit [V0]
- How Patient Became Aware of the NEPTUNE Study
- Final Inclusion Criteria (*requires affirmative response)*: Patient Willingness and Ability to Provide Informed Consent, Willingness to Comply with Study Procedures and Schedule

- Research Coordinator's Assessment of Patient Enthusiasm
- Opportunity to Review Informed Consent on Day of Eligibility Visit or to Schedule
    - If and only if patient signs informed consent – request for the following details:
        - Ethnic Background*
        - Racial Background*

* This information must be entered into Velos CRF 4A upon registration of consented participants for all sites (see Velos MOP).

Informed consent may be obtained at this visit, during the Baseline Visit [V2], or during the Biopsy Visit [V3]; depending on the recruitment strategy at a site. If the individual is prepared to consent and meets all study criteria, [V1] and [V2] can be in succession on the same day (excluding baseline blood draw), as can [V1] and [V3] be in succession on the same day. Please review sections 1.C.2. and 1.C.3 for informed consent procedures.

If consent is given, it is required to assign the participant a study ID and complete the Velos Enrollment (Form 2A) to enroll the consented participant into NEPTUNE. If time permits, the Medication Log, Contact Information, and Healthcare Provider Information, should be started on the respective worksheets (Forms 5, 2B, and 3, in order of priority). Please note a medication log must be started prior to post-biopsy treatment.

4.B.3. Velos Study Participant Registration

Once the following details are complete, the participant is considered enrolled and should be registered into Velos eResearch Data Management System.

- Screening Log updated
- Pre-Screening details reviewed
- Eligibility Assessment Worksheet (Form 1) completed
- Informed Consent documented
- Study Participant ID Number assigned
- Velos Patient ID Number assigned
- Velos Enrollment Worksheet (Form 2A) completed

The Velos Enrollment Worksheet (Form 2A) has been created to assist in the registration process and needs to be completed with the study participant.

4.B.4. Velos Enrollment Worksheet (Form 2A)

Upon consent, the Velos Enrollment Worksheet must be completed as a minimum to enroll the consented participant into the study. This form should be maintained in the local (shadow) research chart and contains the necessary information to register participants into Velos. It includes:

- Name (not entered into Velos, except at lead site)
- Date of Birth
- Gender
- Marital Status
- Blood Type

- Organization (Clinical Site)
- Survival Status
- Study ID
- Study Status and Date
- Patient Study ID
- Protocol Calendar (to populate the appropriate CRFs)
- Patient Start Date

4.B.5. Contact Information (Form 2B)

This worksheet will track a participant's contact information for the duration of the study and will be confirmed at each visit. This information is *strictly* local and should not be shared outside the local recruiting site. This should be maintained in the local (shadow) research chart and kept under lock and key as detailed in the IRB application and informed consent. Details include:

- Full Name (First, Middle, Last)
- Social Security Number
- Home Address (Street, City, County, State/Province, Zip/Postal Code, Country)
- Email Address
- Phone Numbers (Home or cell, Work)
- Next of Kin Contact Information

4.B.6. Healthcare Provider Information (Form 3)

This worksheet and corresponding CRF will track the participant's healthcare providers for the duration of the study and will be confirmed for changes and/or updates at each visit. This information will be entered into Velos as previously described for local and central data entry.

4.B.7. Baseline Concomitant Medications Log (Form 5) and CRF

This worksheet and corresponding CRF will track a participant's medication changes throughout the study. Baseline information should include all prescription medications and non-prescription supplements, vitamins, or other treatments, including dates of start/stop recall, dosage, and route of administration.

4.C. Re-Screening Potential Participants

If a biopsy has been postponed for greater than the 90 day window of eligible 24 hour urine protein or a spot sample, the participant should be re-screened when the biopsy is re-scheduled. If this occurs, please do not re-enter all screening information. If the baseline visit has already taken place, the baseline history and clinical information will need to be recaptured; and the baseline physical exam should be repeated. Additionally, please record the local lab results with the date nearest to the date of the biopsy procedure.

5. Enrollment [V1]

A patient is considered enrolled once the informed consent is obtained. And as outlined above, data entry of Forms 1, 2A/B, 3, 4A (Ethnicity and Race information only) and 5 will conclude [V1].

6. Baseline Visit [V2]

This section of the manual provides a summary of activities and procedures scheduled to occur at the NEPTUNE Baseline Study Visit [V2]. If the Baseline Visit is a combination of [V1/V2] or [V2/V3], it will be necessary to complete a limited Baseline Visit, omitting the baseline blood and possibly the 24 hour urine samples.

In such instances, the sample collection will need to be scheduled for a different date to facilitate fasting for the blood draw. If the participant was previously consented and supplied collection materials for a 24-hour urine, it can be collected with the spot urine sample. If no 24-hour urine collection materials were available prior to the visit, it is recommended both the blood and urine be delayed.

6.A. Limited Visit Overview [V1/V2]

If not already obtained, the Informed Consent Process will take place. If the informed consent is signed at the Baseline Visit [V2], no study procedures should have been initiated, unless prior approval by the local IRB. As a *limited* Baseline Visit [V2], the baseline blood (fasting) and 24 hour urine sample will need to be rescheduled for a different date.

After the informed consent has been reviewed and signed, the individual can be assigned a study ID number and enrolled into the NEPTUNE study.

All sites are responsible for registering their participants into Velos and completing the following Velos Case Report Forms (CRFs):

a. The date Informed Consent was signed

b. The limited data set from the Eligibility Assessment Worksheet (Form 1)

c. The necessary demographic data in the Baseline Participant Information (Form 4A), as these responses are generated from the Eligibility Assessment Worksheet (Form 1)

Baseline activities and information to be acquired from consented participants that are permitted to occur at a [V1/V2] Limited Visit include:

6.A.1. Participant Information, Medical History, and Physical Exam Assessments

Information will be obtained from the participant and recorded on the respective study visit worksheet. Additionally, the treating physician or RC will conduct a limited physical examination to be recorded on the outlined worksheets. (Please see Appendix E for Physical Measurement Instructions).

6.A.1.a. *Baseline Participant Information Worksheet (Form 4A) /CRF*

- **Demographics**
  - Primary Language
  - Ethnic and Racial Background
- **Socio-Economic**
  - Employment
  - Student Status
  - Education Level
  - Gross Annual Income
- **Healthcare Utilization**
  - Emergency Room Visits
  - Hospitalizations

- Health Insurance
- Birth History

- **Next of Kin Information**
  - Parental Education
  - Racial Background of Biological Mother and Father
- **Social History**
  - Drug, tobacco and alcohol use

6.A.1.b. *Baseline Family History Worksheet (Form 4B)/CRF*

- **Family History: Parents, Siblings, Children**
  - Family History of Kidney Disease
  - Family History of Hypertension
  - Family History of Diabetes

6.A.1.c. *Baseline Clinical Information Worksheet (Form 4C)/ CRF*

- **Kidney Disease History**
  - Onset of Kidney Disease Diagnosis
- **Nephrotic Syndrome Treatment History**
- **Renal Replacement Therapy History**
- **Other Medical History**
  - Hypertension, Diabetes, Coronary Artery Disease, Heart Failure, Heart Arrhythmia, Stroke, Thromboembolic Events, Peripheral Vascular Disease, Cancer, Rheumatologic Disease
  - Infection History, including:
    - Hepatitis: A, B, C
    - HIV
  - Transfusion History
  - Clinical Abnormalities:
    - Deafness, Blindness, Microcephaly, Facial Dysmorphy, Mental Retardation, Polydactyly, Spondyloepiphyseal Dysplasia, Male Pseudohermaphroditism, Microcoria, Heart Anomalies, and Cardiomyopathy.
  - Allergies (food, drug, environmental)
  - Puberty and Development Questions
- **Clinical Symptoms**
  - Abnormal Symptoms (Shortness of Breath, Swelling, Fever, Chest Pain, Foamy Urine, Diarrhea, Nausea and Vomiting)
- **Clinical Nephrotic Exam**
  - Weight
  - Height
  - Sitting and Standing Blood Pressure
  - Pulse
  - Periorbital/Facial Edema
  - Lower Extremity Edema
  - Sacral Edema
  - Anasarca

At this visit the RC will also obtain documentation for permission to obtain medical records with appropriate signature(s). Please have participants sign the Authorization to Release Patient Information Form, the Authorization to Request Patient Information Form, as well as your institution's required medical release form.

This information will be updated at annual visits.

6.A.2. Quality of Life Surveys and CRFs

At this visit, participants will be administered surveys including the following:

6.A.2.a. *SF-36 (Adult 36- question Quality of Life)*

- Participants > 18 years
- QOL Surveys Worksheet (Form 6A-E2)
- Velos CRF Form 6A

6.A.2.b. *PedsQL (Pediatric 23-question Quality of Life)*

- Parent / Guardian and Participants < 18 years
- < 8 years to be completed by parent/guardian only
- QOL Surveys Worksheet (Form 6A-E2)
- Velos CRF Form determined by participant age

6.A.2.c. *PROMIS On-line survey (All ages)*

- PROMIS Survey Worksheet (Form 7)
- Velos CRF Form 7

Instructions for administering these surveys are found in Appendix F.

6.A.3. Other biospecimens that may be collected at the Limited [V2] Visit:

Nail clippings will be obtained for studies of heavy metal exposure (See Appendix G for nail collection/processing and sample labeling procedures).

6.A.4. Baseline Labs (Form 10) and CRF

The following local lab results, from within ± 30 days of the Baseline Visit, should be obtained from the participant's medical chart and recorded on the Baseline Labs Worksheet (Form 10).

- CBC [Hemoglobin, Hematocrit, WBC, MCV, MCH, MCHC, Platelets]
- Metabolic panel [Albumin, Bicarbonate, Total Bilirubin, Calcium, Chloride, Creatinine, Glucose, Alkaline Phosphatase, Potassium, Total Protein, Sodium, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Urea Nitrogen, Hemoglobin A1c and Magnesium and Phosphorous if available]
- Urinalysis, Spot Urine Assay, and 24 Hour/timed urine collection

  NOTE: If your institution routinely performs a urine dipstick in the clinic area without transferring this information to the medical record, record the data results of the urine dipstick on the Baseline Labs Worksheet before these data are discarded.

Both the worksheet and CRF contain a field to record the lab value, and a date field to input the date from which the lab value was determined. Please record both parts of the necessary data. For sites completing data entry locally, the CRF defaults to "NA" – which applies to lab results not completed during the course of the participant's clinical care. A value of "0" should only indicate a numerical value of "0".

6.B. Limited Visit Overview [V2/V3]

If not already obtained, the Informed Consent process will take place. If the informed consent is signed at the Baseline Visit [V2] no study procedures should have been initiated, unless prior approval by the local IRB. As a *limited* Baseline Visit [V2] the baseline blood (fasting) and 24 hour urine sample will need to be rescheduled for a different date.

After the informed consent has been reviewed and signed, the individual can be assigned a study ID number and enrolled into the NEPTUNE study.

All sites are responsible for registering their participants into Velos and completing the following Velos Case Report Forms (CRFs):

a. The date Informed Consent was completed

b. The limited data set from the Eligibility Assessment (Form 1)

c. The necessary demographic data in the Baseline Participant Information (Form 4A), as these responses are generated from the Eligibility Assessment Worksheet (Form 1)

Activities and information that will be acquired from the participants that are permitted to occur at a [V2/V3] Limited Visit include all items designated in the Limited Visit Overview [V1/V2] with the addition of the biopsy visit, identified in Section 6.

6.C. Complete Visit Overview [V2]

One week prior to the study visit the RC will mail the participant a visit reminder card that will prompt the patient to come fasted and bring their Medication Diary and Birth History Handout to the visit. Additionally, the RC will call the participant the day before their appointment and remind them to come fasted and bring their Medication Diary and Birth History Handout (See Appendices H & I).

Activities and information that will be acquired from the participants that are scheduled to occur at a [V2] Complete Visit include all items designated in the Limited Visit Overview [V1/V2] with the addition of the fasting blood draw and 24 hour and spot urine samples.

6.C.1. Baseline Biobank Specimens (Form 8) and CRF

The Baseline Visit will include the following biospecimens procurement, to be recorded on the Baseline Biobank Specimens Worksheet (Form 8) and entered into the Velos CRF:

Blood

There will be a 110 cc fasting blood draw for adults at the Baseline Visit (See Appendix J for the blood collection procedures and the Biobank Baseline Blood MOP for blood processing/shipping procedures). Pediatric blood draws will be according to weight as follows in Table 3:

Table 3. Pediatric blood volume draw by weight

Weight	< 20 pounds	21-51 pounds	> 52 pounds
Blood Draw Volume	20cc	50cc	100cc

Adult participants with a hematocrit below 28% and above 25% will have a 50cc fasting blood draw. Adult participants with a clinically measured hematocrit below 25% will not be drawn at a visit ± 30 days from documented hematocrit value.

Pediatric participants > 52 pounds, with a hematocrit below 28% and above 25%, will have a 20cc blood draw. Pediatric participants < 52 pounds with a hematocrit below 28% and above 25%, as well as all pediatric participants with a hematocrit below 15%, will not be drawn.

If the baseline visit occurs on the same day as biopsy visit, the blood draw will be deferred to a subsequent day, but not later than 30 days after the procedure.

Clean Catch Urine

A "clean catch" research urine sample will be collected from all participants. Approximately 50 cc of the "clean catch" urine will be processed and transferred to the NEPTUNE Biorepository (See Appendix K for urine collection procedures and the Biobank-Urine Spot MOP for processing/shipping procedures).

24 Hour Urine/Timed Urine

A 24 hour urine sample will be collected from adult and continent child participants for Protein, Albumin, Creatinine, Urea Nitrogen and Sodium. In children below five years of age, a timed urine will be used and for pediatric participants unable to produce a timed urine, a urine capture will be attempted (See Appendix K for urine collection procedures and the Biobank-Urine 24 hour MOP for processing/shipping procedures).

Other biospecimens

Nail clippings will be obtained for studies of heavy metal exposure (See Appendix G for nail collection/processing and sample labeling procedures).

The data and specimens obtained at the Baseline Visit will serve as the baseline study data for the purpose of data analysis and biochemical investigations and will include collecting detailed participant medical history, limited physical exam assessments, samples for the NEPTUNE, Mayo Urine, and NIDDK Biorepositories, reviewing the medical chart for clinically indicated local lab tests and completing questionnaires.

7. Biopsy Visit [V3]

7.A. Visit Overview

This visit is concurrent with the kidney biopsy procedure.

IT IS ABSOLUTELY PERTINENT THE SITE RC ARRANGE STUDY SPECIFIC DETAILS WITH THE PHYSICIAN PERFORMING THE RENAL BIOPSY

Prior to the biopsy procedure (day of, or up to 7 days preceding), it is essential the RC obtain a small blood sample (10 cc) and a clean catch spot/random urine sample. These specimens will be used as initial study data to provide *pre-treatment* samples of plasma, serum, and RNA profiles.

It is essential the urine sample be obtained *prior* to the biopsy, as any traces of hematuria would be non-interpretable due to the procedure. When necessary, the blood specimens can be obtained same-day, post-procedure. Sample procurement details should be recorded in the V3 Biopsy Specimens Worksheet.

During the clinically indicated renal biopsy procedure, an additional renal biopsy core will be obtained for research purposes. This tissue must immediately be submersed in the NEPTUNE study cryovial with the green-cap, containing RNA-Later. The additional core will be stored with the NEPTUNE RC until it is confirmed that adequate tissue necessary for histologic diagnosis of renal disease has been received, processed, and the treating physician, in consultation with the renal pathologist, has determined there is no longer clinical need for this sample, at which time it will be released for research use in the NEPTUNE Study. The procurement date should be recorded in the Kidney Specimen Form (Form 11A)**.**

Based on the local histological report thereafter, NEPTUNE participants will be assigned into an initial study cohort (FSGS/MCD, MN, or OG) by the Pathology Review Committee. This information will be entered into the Pathology Assignment CRF (Form 12) by the DACC.

7.B. Approaching patients the day of the biopsy and obtaining the biopsy

7.B.1. Potential Participant is being approached for the first time *[V1/V3]*:

Once approval has been obtained to approach the potential participant, the study team member may meet with the potential participant in the relevant pre-biopsy area. The RC will inform the individual about the study and ask if they would like to hear more about the study (See suggested screening language).

If the Potential Participant Agrees:

1. If, at this point, the individual is interested in participating in the study, the RC will complete the second half of the Eligibility Assessment Worksheet (Form 1) with the individual (Review Section 4.B.2.).
2. If the individual is eligible based on the completed Eligibility Assessment Worksheet (Form 1), the overall study details will be discussed with them. The RC will begin the Informed Consent Process (Section 1.C.2 and 1.C.3).
    a. After the informed consent has been reviewed and signed, the individual can be assigned a study ID number and enrolled into the NEPTUNE study.
    b. Initiate the blood specimen collection and the clean catch urine collection, recording details on the proper study document (V3 Biopsy Specimens Worksheet).

c. As time permits, begin the Medication Log, and collect Contact Information, Healthcare Provider Information on the respective worksheets (Forms 2A/B, 3 and 5). **Please note a medication log must be started prior to the biopsy**.

d. The information in Forms 1, 2A/B, 3, and 5, should then be transferred into the Velos CRFs.

Local data entry:	Upon data entry of Forms 1, 2A/B, 3, 4A (Ethnicity and Race information only) and 5 [V1] is now complete.
Central data entry:	Upon completion of Forms 1, 2A/B, 4A (Ethnicity and Race information only) Velos documentation is complete for [V1]. Forms 3 and 5 must be sent to the DACC within 7 days for [V1] completion.

e. The information in Form 11A and V3 Biopsy Specimen, should then be transferred into the Velos CRFs.

Local data entry:	Upon data entry of Forms 11A and V3 Biopsy Specimen, [V3] is now complete.
Central data entry:	Upon data entry of Form 11A Velos documentation is complete for [V3]. V3 Biopsy Specimen must be sent to the DACC within 7 days for [V3] completion.

3. Provide the patient information about the NEPTUNE Registry and The NephCure Foundation and answer any questions they may have about the registry study.
4. Schedule or complete the limited elements of the Baseline Visit [V2] if time permits.
5. If the individual is not eligible based on the completed Eligibility Assessment Worksheet (Form 1), thank them for considering the study and for their time.
   a. Provide the patient information about the NEPTUNE Registry and The NephCure Foundation and answer any questions they may have about the registry study.
   b. Provide a brief follow-up so they know they are valued as patients and have a conclusive response from the study.
6. PLEASE REMEMBER TO RECORD THIS INFORMATION ON THE SCREENING LOG AT YOUR SITE.

<u>If the Potential Participant is Not Interested or Ineligible:</u>

1. If the potential participant is ineligible or uninterested in the study, thank them for considering the study and for their time.
2. Provide the patient information about the NEPTUNE Registry and answer any questions they may have about the registry study.
3. Provide a brief follow-up so they know they are valued as patients and have a conclusive response from the study.
4. PLEASE REMEMBER TO RECORD THIS INFORMATION ON THE SCREENING LOG AT YOUR SITE.

7.B.2. Participant Has Completed Screening/Eligibility and Baseline Visits ([V3] only):

The participant will be approached in clinic by the RC who will again thank them for participating in the study. The RC should be present during the biopsy procedure to collect the additional

core. Alternatively, the RC may be contacted to retrieve the additional core immediately following the procedure. The additional core will be stored with the NEPTUNE RC until it has been confirmed by the Pathologist that adequate tissue has been obtained for histologic diagnosis. The procurement date should be recorded in the Kidney Specimen Form (Form 11A) and in the Velos for both local and central data entry sites.

Meet your consented participant at "Pre-Op" facility or previously agreed upon meeting point:

1. Greet your participant and thank them for participating in NEPTUNE.
2. Initiate the blood specimen collection and the clean catch urine collection, recording details on the proper study document (V3 Biopsy Specimens Worksheet)
3. As time permits, begin the Medication Log, and collect Contact Information, Healthcare Provider Information on the respective worksheets (Forms 2A/B, 3 and 5). **Please note a medication log must be started prior to the biopsy**.
4. The information in Form 11A and V3 Biopsy Specimen, should then be transferred into the Velos CRFs.

Local data entry:	Upon data entry of Forms 11A and V3 Biopsy Specimen, [V3] is now complete.
Central data entry:	Upon data entry of Form 11A Velos documentation is complete for [V3]. V3 Biopsy Specimen must be sent to the DACC within 7 days for [V3] completion.

7.B.3. Biopsy Occurs Prior to Potential Participant Contact:

At some institutions an additional biopsy core will be obtained in RNA-Later as part of routine clinical procedure. If this is the case, and approval has been obtained to approach the potential participant, the participant may be contacted about the study following the collection of the biopsy tissue. The RC will inform the potential participant about the study and ask if they would like to hear more about the study.

Discuss with Matthias regarding window for obtaining V3 specimens?

If the Potential Participant Agrees:

1. If the individual agrees, the study will be discussed with them at length.
2. If, at this point, the individual is interested in participating in the study, the RC will complete the second half of the Eligibility Assessment Worksheet (Form 1).
3. If the individual is eligible to participate in the study, the RC will begin the Informed Consent Process (Section 1.C.2 and 1.C.3).
4. After the informed consent has been reviewed and signed, the individual can be enrolled onto study using VELOS and the Eligibility Assessment Worksheet can be entered into the Eligibility Assessment Case Report Form in VELOS.
5. Also, after the informed consent has been signed the RC may acquire the additional core, which has already been collected, process the core according to instructions (Please see Specimen Processing MOP) and complete the Kidney Specimens Worksheet (Form 11A) and Velos Case Report Form.

If the Potential Participant is Uninterested or Ineligible:

1. If the potential participant is ineligible or uninterested in the study, thank them for considering the study and for their time, and provide a brief follow-up so they know they are valued as patients and have a conclusive response from the study.
2. PLEASE REMEMBER TO RECORD THIS INFORMATION ON THE SCREENING LOG AT YOUR SITE

7.C. Biopsy Sample Processing/Shipment

The additional renal core should be shipped with the biopsy visit [V3] samples on dry ice to the NEPTUNE Biobank Core. No processing is necessary for the biopsy core, other than receiving site pathologist and treating physician release of tissue for research. Blood and urine biospecimens should be recorded in the V3 Biopsy Specimens document and processed according to the blood and spot/random urine protocols. (Please see Appendix L, Biospecimen processing for further details).

8. Pathology Materials

Each site will be provided with a slide pathology kit for each participant and on-line access for shipping.

Detailed instructions are provided in the Pathology Manual of Procedures - MOP (Appendix B). Requested pathology materials should be shipped to the NIDDK as outlined.

8.A. Materials Requested

NEPTUNE is requesting the following processed and unprocessed slides:

- Glass slides:
  - All Light Microscopy (LM) glass slides clinically processed and available for LM
  - Thick sections of tissue processed for Electron Microscopy (EM)
  - H & E from frozen sections of tissue processed for Immunofluorescence
  - Unstained slides: 4 are requested

- EM Material:
  - CD with copy of digital EM images (preferred)
  - Or, CD with locally scanned EM images
  - Or, EM Prints

- Immunofluorescence (IF) Material:
  - CD with IF images if available and with pathology report

- Pathology Report
  - Electronic copy of de-identified pathology report
  - Or, hard copy of de-identified pathology report

Research Coordinators will be provided with a specific "Slide Pathology Kit" for each NEPTUNE participant, including the following materials:

- De-identifying labels
- Glass Slide Cases
- Blank CD with NEPTUNE Study ID label
- Padded envelopes for sending/receiving materials to the NIDDK Histopathological Archive

Detailed instructions for preparing slides, digital images or prints, and de-identifying documents are located in the Pathology Manual of Procedures (Appendix B***).***

Additionally, the sites are encouraged to provide a full copy of bound Pathology Manual of Procedures to the local pathology departments to disclose and share the NEPTUNE study goals regarding the pathology request. No additional processing is requested by any site further than staining done for standard clinical care. Stained slides will be returned.

9. Follow-Up Visits [V4-V13]

9.A. Visit Overview

Follow-Up Visits in year one will occur in person at four-month intervals (months 4 and 8) based on the Baseline Visit [V2]. Thereafter, Follow-Up Visits will occur at six-month intervals for the remainder of the study. Participants may be contacted by phone as necessary between visits to update contact information, ascertain interim medical history and potential outcomes of events, and assess health resource utilization. Follow-Up Visits are expected to occur within a range of one month before and up to one month after the visit timeline according to the visit calendar.

9.B. Medical History Update and Physical Exam Assessments

Information will be obtained from the participant and recorded on the respective study visit worksheet. Additionally, the treating physician or RC will conduct a limited physical examination which will include the following measurements to be recorded on the outlined worksheets and Velos Case Report Forms (Please see Appendix E for Physical Measurement instructions).

Information from worksheets will be transferred into the corresponding Velos Case Report Form (CRF) within one week. The following information will be acquired from the participants and recorded on the outlined worksheets and VELOS Case Report Forms:

9.B.1. Follow-Up Participant Information Worksheet (Form 13A) and CRF

- **Healthcare Utilization**
  - Interim Emergency Room Visits
  - Interim Hospitalizations
  - Health Insurance Updates
- **Social History**
  - Drug, tobacco and alcohol use
- **Socio-Economic Information**
  - Employment Updates
  - Student Status Updates
  - Gross Annual Income Changes
- **Social History**
  - Drug, tobacco and alcohol use

9.B.2. Follow-Up Family History Worksheet (Form 13B) and CRF

- **Family History**
  - Interim Diagnosis of Kidney Disease
  - Interim Diagnosis of Hypertension
  - Interim Diagnosis of Diabetes

9.B.3. Follow-Up Clinical Information Worksheet (Form 13C) and CRF

- **Interval History**
  - Hypertension, Diabetes, Coronary Artery Disease, Heart Failure, Heart Arrhythmia, Stroke, Thromboembolic Events, Peripheral Vascular Disease, Cancer, Rheumatologic Disease
  - Transfusions
  - Interim Infections, Including:
    - Hepatitis: A, B, C
    - HIV

- New Allergies
- Puberty Questions
- Renal Replacement Therapy and Kidney Transplant Information

- **Clinical Symptoms**
  - Abnormal Symptoms (Shortness of Breath, Swelling, Fever, Chest Pain, Foamy Urine, Diarrhea, Nausea and Vomiting)

- **Clinical Nephrotic Exam**
  - Sitting and Standing Blood Pressure
  - Pulse
  - Weight
  - Height
  - Presence of Ascites
  - Lower Extremity Edema
  - Periorbital/Facial Edema
  - Sacral Edema
  - Anasarca

On a yearly basis the RC will need to update each participant's permission to obtain medical records with appropriate signature(s). Please have participant's sign the Authorization to Release Patient Information Form, the Authorization to Request Patient Information Form, as well as your institutions required medical release form.

One week prior to the study visit the RC will mail the participant a visit reminder card (depending on site practice) that will prompt the patient to come fasted and bring their Medication Diary and Birth History Handout to the visit. Additionally, the RC will call the participant the day before their appointment and remind them to come fasted and bring their Medication Diary and Birth History Handout.

9.C. Concomitant Medications Log (Form 5) and CRF

Updates to this worksheet and corresponding CRF are essential. This documentation will track a participant's medication changes throughout the study. Follow-up information should include any changes in a participant's prescription medications and non-prescription supplements, vitamins, or other treatments, including dates of start/stop recall, and dosage.

9.D. Quality of Life Surveys

The population respective Quality of Life questionnaires (SF-36, Peds QL and PROMIS) should be administered at [V4] and subsequently on an annual basis beginning with [V6]. Answers from the questionnaires should be transferred within one week into the corresponding Velos Case Report Forms.

Instructions for administering these surveys are found in Appendix F. Please transfer questionnaire answers to the corresponding Velos CRFs within one week.

PROMIS surveys will be directly entered by each participant. There is no related worksheet or source documentation.

9.E. Follow-Up Biorepository Specimens

The Follow-Up Visits will include the following biospecimen procurement, to be recorded on the Follow-Up Biobank Specimens Worksheet (Form 14) and Velos CRF:

Blood

There will be a 65 cc fasting blood draw for adults at each Follow Up Visit (See Appendix J for the blood collection procedures and the Biobank Follow-Up Blood MOP for blood

processing/shipping procedures). Pediatric blood draws will be according to weight as follows in Table 3:

Table 3. Pediatric blood volume draw by weight

Weight	< 20 pounds	21-51 pounds	> 52 pounds
Blood Draw Volume	20cc	50cc	65cc

Adult participants with a hematocrit below 28% and above 25% will have a 20cc fasting blood draw. Adult participants with a clinically obtained hematocrit below 25% will not be drawn.

Pediatric participants > 52 pounds, with a clinically obtained hematocrit below 28% and above 25%, will have a 20cc blood draw. Pediatric participants < 52 pounds with a hematocrit below 28% and above 25%, as well as all pediatric participants with a hematocrit below 25%, will not be drawn.

Clean Catch Urine

A "clean catch" research urine sample will be collected from all participants at all Follow-Up Visits. Approximately 50 cc of the "clean catch" urine will be processed and transferred to the NEPTUNE Biorepository (See Appendix M for urine processing procedures).

24 Hour Urine/Timed Urine

A 24 hour urine sample will be collected from adult and continent child participants when possible. This sample will be assessed for Protein, Albumin, Creatinine, Urea Nitrogen and Sodium. In children below five years of age, a timed urine will be used and for pediatric participants unable to produce a timed urine, a urine capture will be attempted (See Appendix K for urine collection procedures and the Biobank-Urine 24 MOP for processing/shipping procedures).

Other biospecimens

Nail clippings will be obtained for studies of heavy metal exposure at Follow-Up Visits [V6], [V8], [V10], [V12], and [V13]. (See Appendix G for nail collection/processing and sample labeling procedures).

9.F. Local Lab Tests

In addition to the biorepository specimens, the following local lab results, from within the previous to post (+/-) 30 days, should be obtained from the participant's medical chart and recorded on the Follow-Up Labs Worksheet (Form 15) at each Follow-Up Visit. Information from the worksheet should be transferred within one week to the VELOS Follow-Up Labs Case Report Form:

- CBC [Hemoglobin, Hematocrit, WBC, MCV, MCH, MCHC, Platelets]
- Metabolic panel [Albumin, Bicarbonate, Total Bilirubin, Calcium, Chloride, Creatinine, Glucose, Alkaline Phosphatase, Potassium, Total Protein, Sodium, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Urea Nitrogen, Hemoglobin A1c and Magnesium and Phosphorous if available]
- Urinalysis, Spot Urine Assay, and 24 Hour/Timed Urine.

  NOTE: If your institution routinely performs a urine dipstick in the clinic area without transferring this information to the medical record, record the data results of the urine dipstick on the Baseline Labs Worksheet before these data are discarded.

Both the worksheet and CRF contain a field to record the lab value, and a date field to input the date from which the lab value was determined. Please record both parts of the necessary data. The CRF defaults to “NA” – which applies for lab results which have not been completed during the course of the participant’s clinical care. A value of “0” should only indicate a numerical value of “0”.

10. Participant Withdraw/Death and Study Completion

10.A. Withdrawing Participants from Study

If a participant officially or unofficially (participant can no longer be reached via the usually methods of contact) withdraws from the study, record this in Velos by changing the 'Study Status' for that participant. The status is changed by selecting a participant and adding a new status under the Screening/Enrollment tab. Please see the Velos Manual of Procedures for step-by-step instructions. Participant withdrawal should also be noted in the participant's research chart in the form of a Note to File. Reasons for withdrawal include participant death, loss to follow-up, illness or unwillingness to participate.

10.A.1. Sample Destruction

Participants also have the right to request that their stored specimens be destroyed at any point during the study. The RC will complete a Participant Specimen Withdraw Form with the participant. The participant should be asked about each type of stored specimen (serum, DNA samples, urine and nail specimens). Both the RC and the participant should sign the bottom of the form and this form should be kept in the participant research chart, in a locked cabinet. The RC will also complete a NEPTUNE Specimen Withdraw Form. On this form, the RC will record the participant study ID and those samples to be destroyed. Both the site RC and PI will sign the bottom of this form. The RC will fax the original NEPTUNE Specimen Withdraw Form and to the NEPTUNE DACC and maintain the form in the participant research chart. The NEPTUNE project manager or laboratory manager will ensure that the correct samples are destroyed. Following sample destruction, the person responsible will sign off on the original NEPTUNE Specimen Withdraw Form and keep this form in a designated area in the NEPTUNE Biobank.

10.B. Participant Death

All participant deaths must be reported within 24 hours of learning of the event. Please refer to section 12 for adverse event reporting details.

All deaths should be captured in Velos by changing the participant's 'Study Status'. Participant status is changed by selecting a participant and adding a new status under the Screening/Enrollment tab. Participant withdrawal should also be noted in the participant's research chart in the form of a Note to File. A withdrawal CRF must also be completed in Velos; please see the Velos Manual of Procedures for step-by-step instructions.

RC must make due diligence to obtain a death certificate and/or autopsy report of the deceased individual. Death certificates and autopsy reports should be maintained in the participant's research chart.

10.C. Participants Lost to Follow Up

The RC should make due diligence to contact participants whom miss scheduled follow-up visits. In the event that a participant is lost to follow up the RC will record this information in the participant research chart. Additionally, this should be captured in Velos by changing the participant status.

10.D. Study Completion

When the participant completes the final study visit (Visit 13) or withdraws from the study, the RC should create and sign a note to file that states why and when the participant has completed the study. This note to file should be stored in the participant research chart. Additionally, the participant status should be updated in Velos. Participant status is changed by selecting a participant and adding a new status under the Screening/Enrollment tab.

11. Participant Transfers

11.A. Permanent Participant Transfers

It is possible to permanently transfer a NEPTUNE study participant from one NEPTUNE clinical center to another during the course of the study; however it is preferred that the participant complete the study at the institution that registered the participant.

If it is necessary for a participant to transfer to another clinical center, the RC from the transferring institution should notify the NEPTUNE DACC of the transfer. The transferring institution will maintain their portion of the participant research chart and should include in the chart a Note to File describing the transfer. The institution receiving the participant will begin a new participant research chart and will maintain the unique Participant Study ID assigned by the registering institution. The receiving institution will use this Participant Study ID on all study related worksheets/CRFs and communications regarding the participant.

Communication and sharing of relevant participant information is permitted between the two institutions so long as the Authorization to Release Patient Information form has been signed by the participant.

11.B. Temporary Participant Transfers

It is also possible to temporarily transfer a NEPTUNE Study participant for a random visit to another NEPTUNE clinical center. In this instance, so long as the Authorization to Release Patient Information form has been signed by the participant, the transferring institution will obtain all relevant information regarding the visit from the receiving institution. The transferring institution will maintain this information in the participant research chart and will include a Note to File describing the temporary transfer. Additionally, the transferring institution should notify the NEPTUNE Study Office of the temporary transfer.

12. Adverse Event Reporting

12.A. Reportable Adverse Events

The Rare Diseases Clinical Research Network defines an adverse event as: "…an unfavorable and unintended sign, symptom or disease associated with a participant's participation in a Rare Diseases Clinical Research Network study." In addition, the NEPTUNE protocol requires reporting of serious, non-serious and expected events.

Only those events associated with the conduct of the study and as defined above are reportable. Reportable events will be captured on the Adverse Event Worksheet (Form 9) and in Velos.

All reported Adverse Events will be classified using the Common Terminology Criteria for Adverse Events (CTCAE), version 3, developed and maintained by CTEP at National Cancer Institute.

Prior to submitting an AE form in Velos, please consult with the NEPTUNE DACC to determine the nature of the AE, as well as the severity for the purposes of the study.

12.B. Serious Adverse Events

Serious Adverse Events include those events that: "result in death; are life-threatening; require inpatient hospitalization or prolongation of existing hospitalization; create persistent or significant disability/incapacity, or a congenital anomaly/birth defects."

Within 24 hours (of learning of the event), investigators must report any reportable Serious Adverse Event (SAE) that are considered life-threatening/disabling, result in death of the subject, or are unexpected/unanticipated by phone to the NEPTUNE Study Office. All other SAEs must be reported within 5 working days of learning of the event to the NEPTUNE Study Office.

SAEs should be captured, the day of reporting, on the Adverse Event Form (Form 9) and in Velos.

Local institutional reporting requirements to IRBs, any GCRC oversight committee and the FDA, if appropriate, remain the responsibility of the treating physician and the Study Chair.

12.B.1. Non-Serious Unexpected Adverse Events

Unexpected Adverse Events are defined as any adverse experience(s)…the specificity or severity of which is not consistent with the risks of information described in the protocol.

12.B.2. Non-Serious Expected Adverse Events

Expected Adverse Events are those that are identified in the research protocol as having been previously associated with or having the potential to arise as a consequence of participation in the study.

Non-serious expected events, observed by the participant, RC or investigator, must be reported to NEPTUNE within 20 working days of the notification of the event.

These events will be presented in a tabular form and given to the MRO and RDCRN DSMB on an annual basis. Local site investigators are also required to fulfill all reporting requirements of the local institutions.

13. Site Visits

Each institution will be monitored by site visit at least once per funding cycle. More than one site visit per funding cycle may occur if necessary. At the site visit, the patient's research chart and source documents will be reviewed. Additional site training may also occur at these visits.

Site visits will be arranged at least two weeks in advance and all patient study data is expected to be up to date at the time of review.

Nephrotic Syndrome Study Network (NEPTUNE)

Velos Training Manual

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What is Velos?

Velos eResearch is a commercially-developed, regulatory-compliant, web-based research data management system that allows researchers to efficiently design protocols, track consents, coordinate schedules, and collect and manage data. It uses cutting-edge web technology so research can be conducted in the clinic, the home and the community by offering Study Administration; Clinical Data, Account, Protocol and Patient Management; as well as IRB Review and Monitoring; Data and Safety Monitoring; Financials; and Reporting. Built-in protections promote adoption of industry best practices while enforcing regulatory compliance, such as FDA 21 CRF Part 11 and HIPAA's security and privacy requirements that are governed by HIPAA's "minimum necessary" principle.

Velos eResearch Hardware and Software Requirements and Configuration

I. Requirements Hardware

Listed below are the recommended equipment used with the Velos eResearch Application.

Notes:

1. Minimum requirements for workstations and laptops assume that the equipment is running only Velos applications.
2. Specifications of a workstation or laptop should be determined based on the number of applications running concurrently and the desired performance level of each application being run.
3. While Intel specifications are provided, a processor of equivalent or greater capabilities from another manufacturer, such as AMD, is satisfactory

Item	Recommended
Windows PC or Laptop	Intel Core2 Duo Processor or better, 1GB RAM or higher or equivalent
Mac	Intel Core2 Duo Processor or better; 1GB RAM or higher
Tablets	Not Officially Supported
Printers	Standard office printer
Internet Connection	1500 Kbps (up/down) or higher

A. Software

The following table indicates the supported software and hardware/software combinations. Any issues with the use of the Velos application in a configuration that is not supported are the responsibility of the user or customer.

Notes:

1. If pop-up blocker software is installed on workstations or laptops, it must be configured to allow the Velos eResearch address or website
2. IE is not supported on Mac machines

Software Table

Software	Equipment	Versions Supported
Internet Explorer	Windows machines only	Version v6.x, v7.x
Mozilla Firefox	Windows machines or Mac	Version 2.x and higher
Safari	Mac	Version 2
Anti-Virus Software	Any reputable software, e.g. McAfee, Norton, etc.	Optional; Recommended for users who will be uploading files from an external source that will be stored in the application

NEPTUNE Velos Training Requirements

1. **Velos 100: Introduction to Velos for New Users**

   A web-based training course and prerequisite to acquiring a Velos account in the UM Velos training database. It provides a high level overview of basic navigation, data entry and managing your password and e-signature. (about 45 min)

Request access to the Velos 100 course by providing Ellen Woodard (email: erhw@umich.edu or phone: 734-763-4273) with your full name and uniquename (or full name and email address for off-site users). A web link to the course will then be provided via email.

2. **Patient Management Online Courses at Velos Customer Corner**

   Go to http://cc.veloseresearch.com and sign in to Velos Customer Corner:

   Username: michuser
   Password: mich1234

   PLEASE do **NOT** share the Michigan Velos Customer Corner log on information (i.e., user-name and password) with anyone else!!!!

   In the Main Menu on the left-hand side of the screen, click the "Online Courses" link under "Training" and view the following courses in the "Patient Management" section by clicking the name of the course:

   a. Add a Patient (1:10 min)
   b. Patient Search (2:58 min)
   c. Add & Enroll a Patient (2:01 min)
   d. Enroll Patients (1:35 min)
   e. Manage Patient Schedule (3:24 min)
   f. Enter Patient Forms (2:35 min) (total time about 15 min)

Upon completion of items 1 and 2, contact Ellen Woodard (contact information above) to request access to the Velos training database. Once granted, an automatic email will be sent from Velos containing log on information.

3. **NEPTUNE Hands-on Homework / Certification Test**

   Using the Velos training database, a self-guided, hands-on, step-by-step process to learn how to register patients to Velos, enroll patients in the study, link patients to the study calendar, and enter demographic and CRF data for enrolled patients. Step-by-step guide begins on page 6. (about 60-90 minutes)

Upon completion of item 3, fill out the NEPTUNE Velos Training Completion Record (page 5) and fax to the NEPTUNE Study Office (734-615-6005). Upon verification of homework / certification completion (with a passing score), access to the Velos production database will be granted and an automatic email will be sent from Velos containing log on information. User will then be certified and eligible to begin enrolling patients in the study.

NEPTUNE Velos Training

Completion Record

Please fax this completed form to the NEPTUNE Study Office: (734) 615-6005

		Date:	
Name:			
Title:			
Phone:		**Email:**	
Site:			

Training Item	Date Completed
☐ Velos 100: Introduction to Velos for New Users	
Patient Management Online Courses at Velos Customer Corner:	
☐ Add a Patient	
☐ Patient Search	
☐ Add & Enroll a Patient	
☐ Enroll Patients	
☐ Manage Patient Schedule	
☐ Enter Patient Forms	
☐ NEPTUNE Hands-on Homework / Certification Test	
Patient Study IDs of two new patients enrolled in Velos:	
Patient Study ID of one existing patient enrolled in Velos:	
Patient Study ID of one patient with completed CRFs:	

NEPTUNE Study Office Use Only:

Date Received:		Certification CRF Checked by:			
	☐ Passed	☐ Failed	Score:		
	Retake Date:		Score:		
Date Production Request Submitted:		by:			
Date Production Access Granted:					
Date User Notified:		by:			
Date Added to Study Team:		by:			

NEPTUNE Hands-on Homework / Certification Test

Prerequisites

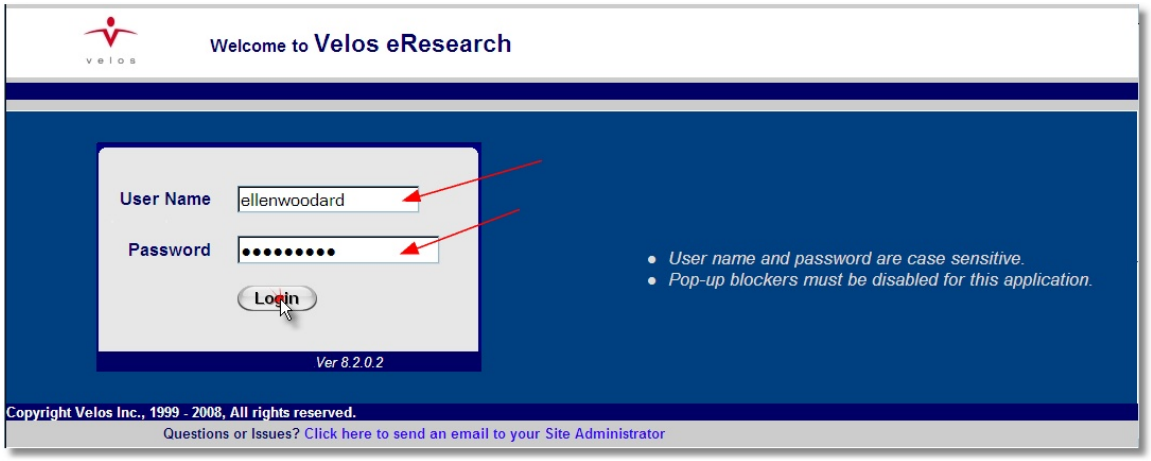
1. Velos 100: Introduction to Velos for New Users
2. Patient Management Online Courses at Velos Customer Corner
3. Access to Velos training database

Learning Objectives

1. Register patients to Velos
2. Enroll patients in a study
3. Link patients to the study calendar and add an unscheduled event
4. Enter demographic and CRF data for enrolled patients

A. Sign in to the Velos training database

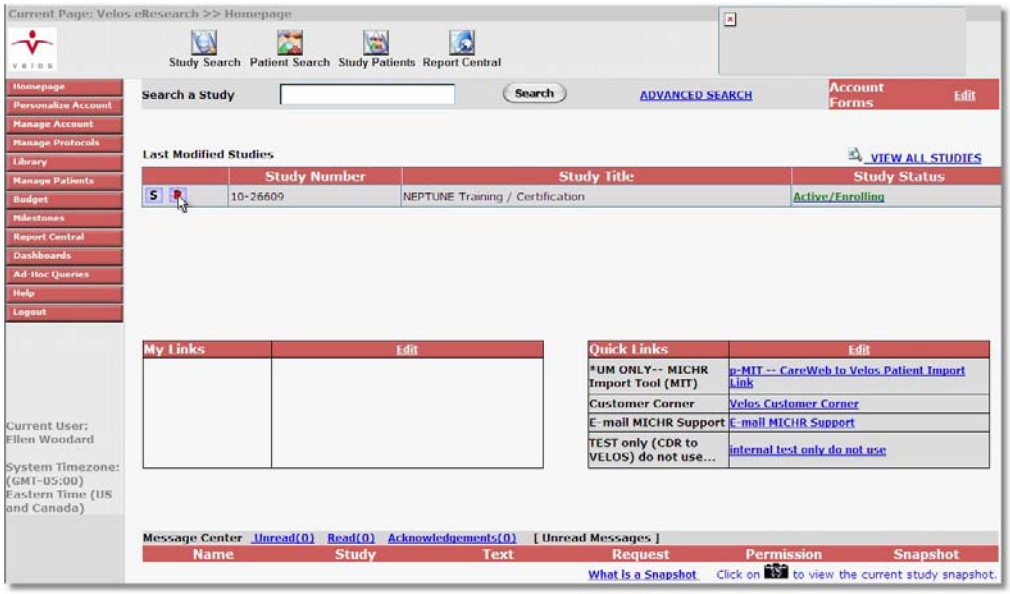
1. Go to https://velostraining.med.umich.edu/eres/jsp/ereslogin.jsp
2. Enter User Name and Password (provided by Velos via email)
3. Click the "Login" button



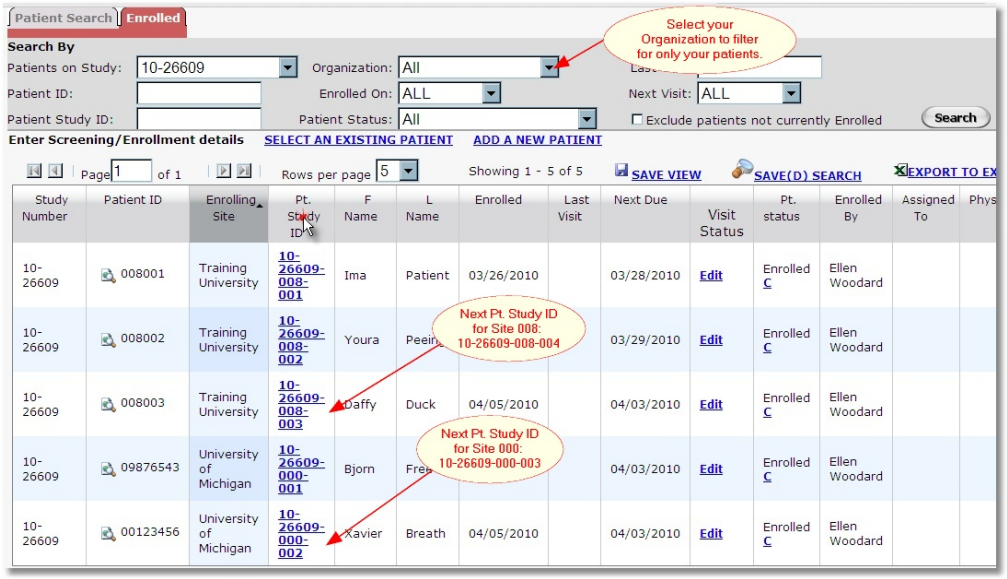
Throughout Velos you are required to enter your e-signature and click a "submit" button any time you've selected, entered and/or changed data. It is important to click the "submit" button only **one** time, then await a screen refresh while the message "processing your request" displays and/or appearance of a message indicating "data saved successfully" (or something similar) before continuing.

B. Enroll at least 3 patients (2 new, 1 existing) in the NEPTUNE Training / Certification study

1. From your Homepage, click the "P" icon to the left of the NEPTUNE Training / Certification study (Study Number 10-26609).



A list of patients currently enrolled in the study (if any) appears. Sort the list of enrolled patients by clicking the "Pt. Study ID" column heading; once for ascending order and again for descending order. Click the arrow buttons above the left-hand side of the list to navigate to additional pages. You can filter the list to show only those patients from your site by selecting your organization ("University of Michigan" for UM users or "Training University" for users from sites outside UM) in the "Organization" dropdown box then clicking the "Search" button. **Make note of the next Patient Study ID for your site.**



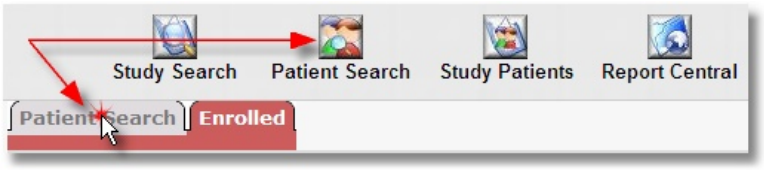
In the Velos production database, you will select your actual organization (i.e., your site – University of Michigan, Montefiore, etc.) in the "Organization" dropdown box to filter the patient list to show only those patients from your site.

ALWAYS make note of the next Patient Study ID for your site. Velos will not automatically generate the Patient Study ID and while in the process of enrolling a patient, you will not be able to go back and check what the next Patient Study ID should be.

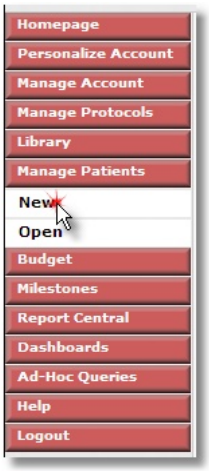
Enroll a New Patient

Velos is a patient-centric database, meaning a unique patient and associated demographics data is entered into Velos only once. It is extremely important not to enter a patient into Velos that already exists in the system. Duplicate patients will result in the need for a time-consuming technical intervention to correct, and always results in the need to re-enter data for that patient. Therefore, **always search for a patient to verify they do not exist in the system before entering them into Velos**. For the purposes of training / certification, this search is not necessary; however, always search for a patient before entering them in the Velos production database.

Access to the patient search screen is obtained by clicking the Patient Search tab (from the screen showing patients enrolled in the study – see step 1, on page 7) or by clicking the Patient Search Icon, which is always present at the top of the Velos screen.



2. After conducting a patient search to verify the patient does not already exist (not necessary for training / certification), register the new patient to Velos by clicking the "Manage Patients" link, then "New" link on the menu bar at the left-hand side of the screen.



3. In the window that appears, enter/select the following information (for the purposes of training / certification, you can make up this information):

   a. Patient ID – for UM, this is the UMH CPI number. Sometimes this number begins with a leading zero, which must be included in Velos. For sites outside UM, this is a six-digit number comprised of the site number (see table, below) and an incremental number for each site, including leading zeros, beginning with 001; e.g., the first patient enrolled at NYUMC would have a Patient ID of 001001; the second patient, 001002; etc.. This number serves as the Velos Patient ID (if you enter a duplicate Patient ID, a message will appear when you leave this field – correct your entry or if correct, search for this patient as they are already entered in the system).

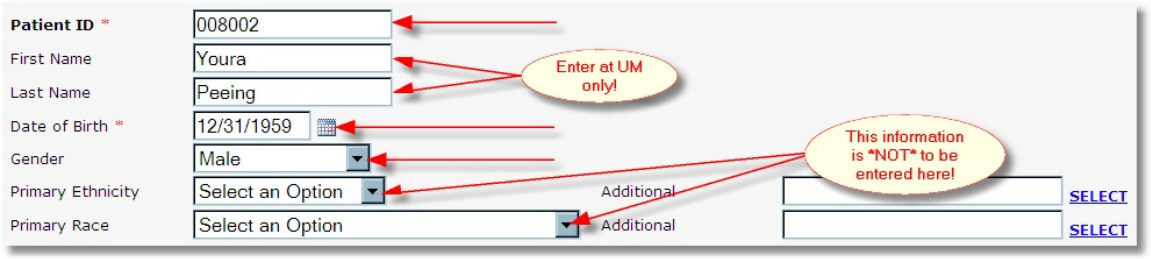
Site	Site ID
University of Michigan	000
NYUMC	001
Johns-Hopkins	002
Toronto	009
Case Western Reserve University	020
Children's Hospital – LA	021
Harbor – UCLA	022
Long Island Jewish	023
Mayo	024
Montefiore	025
University of Miami	026
University of North Carolina	027
University of Pennsylvania	028
University of Washington	029
NIDDK Intramural	030

   b. Date of Birth – click the calendar icon to select the date

   c. Gender – select from the dropdown box

*To protect external site PHI, enter First Name and Last Name in this window at **UM only**.*

*Do **NOT** enter Primary Ethnicity and/or Race in this window – this data is collected elsewhere.*



4. Under “Registration Details,” UM users verify that "University of Michigan" is selected in the "Organization" dropdown box. All users from sites outside UM verify that "Training University" is selected in the "Organization" dropdown box.

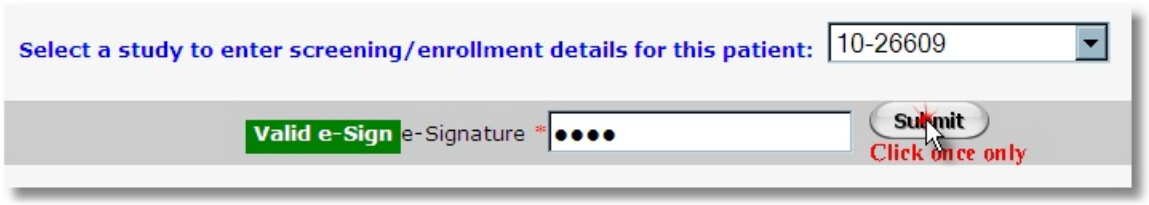
In the Velos production database, you will select your actual organization (i.e., your site – University of Michigan, Toronto, etc.).

Verify that “Alive” is selected in the “Survival Status” dropdown box and for sites **outside UM only**, enter the patient’s medical record number from your institution in the “Patient Facility ID” field (for the purposes of training / certification, you can make up this number).

5. Please do **NOT** make any selection for the Select Specialty link:

6. Scroll down and select "10-26609" (the NEPTUNE study number) from the "Select a study . . ." dropdown box.

7. Enter your e-Signature and click the "Submit" button.



8. In the "Patient Study Status" window that appears, enter the following mandatory data (designated by red asterisks):
   a. Status – select "Enrolled" from the dropdown box.
   b. Status Date – click the "Select Date" link and select today's date (or whatever date you wish to record as the date the patient was enrolled in the study).
   c. Patient Study ID – defaults to the patient's Velos Patient ID. **Change this number** to match the formula YR-IRB#-Site#-### as follows:
      1) YR = last 2 digits of the current year/year patient enrolled in the study (e.g., 10 for a patient enrolled in 2010, 11 for a patient enrolled in 2011, etc.)

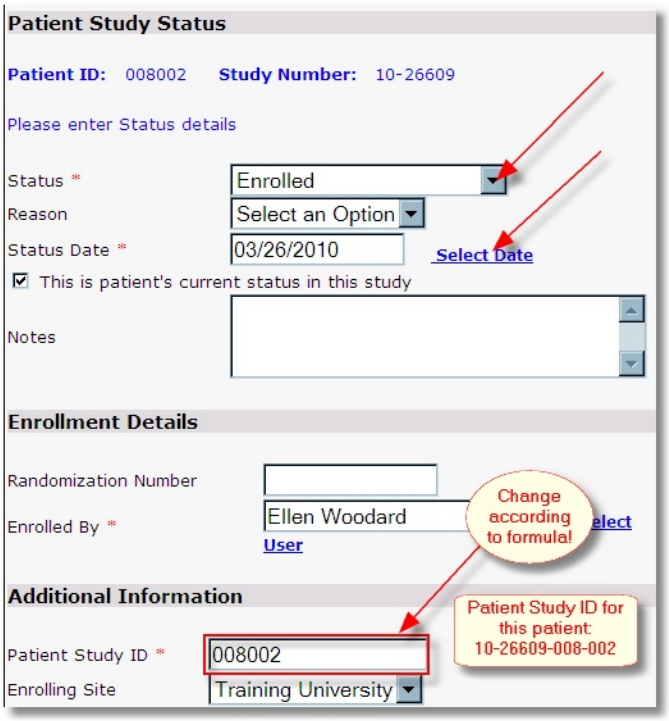
2) UM's IRB# = 26609

3) Site# per the following table:

Site	Site ID
University of Michigan	000
NYUMC	001
Johns-Hopkins	002
Toronto	009
Case Western Reserve University	020
Children's Hospital – LA	021
Harbor – UCLA	022
Long Island Jewish	023
Mayo	024
Montefiore	025
University of Miami	026
University of North Carolina	027
University of Pennsylvania	028
University of Washington	029
NIDDK Intramural	030

4) ### = incremental number for each site, including leading zeros, beginning with 001.

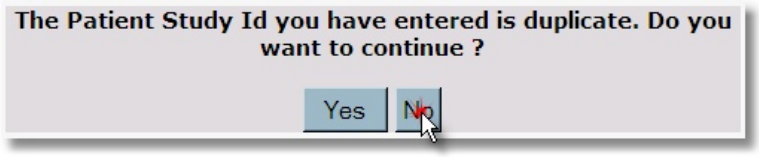
For example, the first patient enrolled at the UM site would have the Patient Study ID 10-26609-000-001; the second patient enrolled at the UM site would have the Patient Study ID 10-26609-000-002, etc.



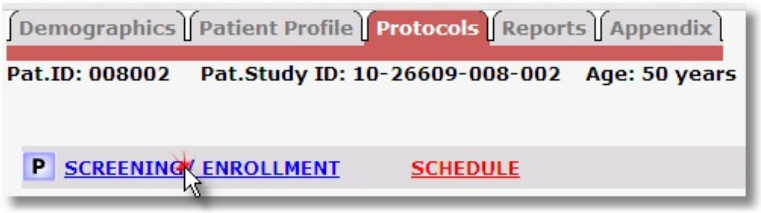
It is not necessary to enter or change any other information in this window.

9. Scroll down to enter your e-Signature and click the "Submit" button.

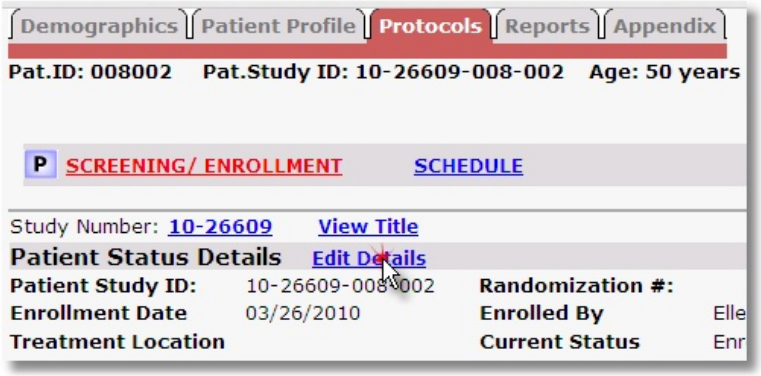
If you entered a duplicate Patient Study ID, an error message will appear. Click "No" (to avoid creation of a duplicate ID) and the Patient Study Status window will reappear. Enter a non-duplicate Patient Study ID, scroll down to enter your e-Signature and click the "Submit" button.



If, for any reason, you find it necessary to return to the "Patient Study Status" window, click the "Screening/Enrollment" link on the "Protocols" tab of the "Manage Patient" section.



Then click the "Edit Details" link next to "Patient Status Details."

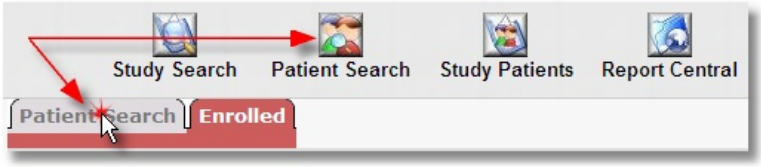


You are now done registering a new patient to Velos and enrolling them in the study.

Go back to step 2, beginning on page 8, to enroll a second new patient or if you have already enrolled two new patients, continue to the next step.

Enroll an Existing Patient

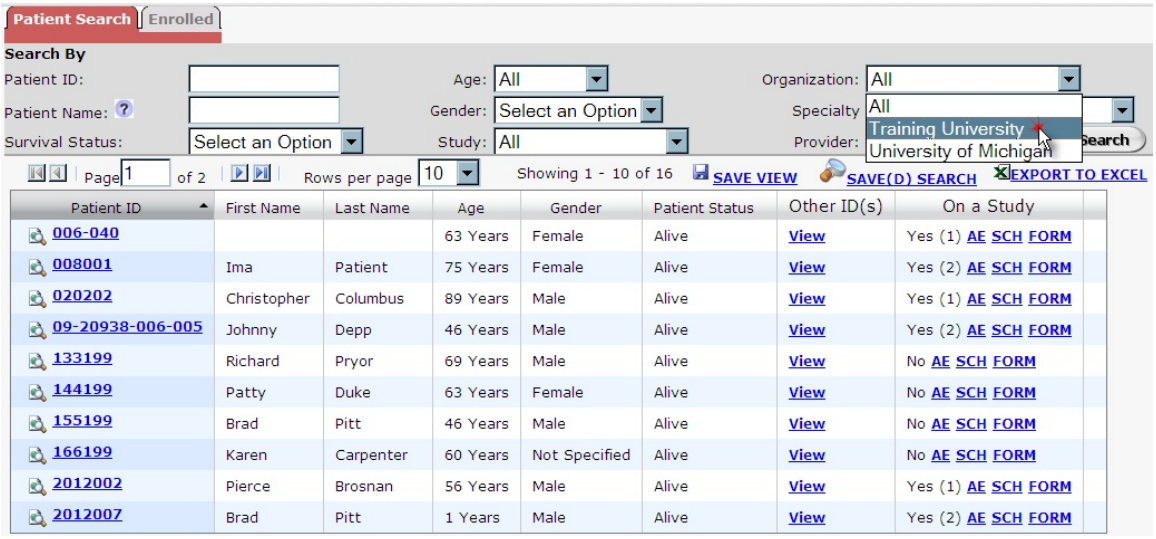
10. Search for a patient already registered in the Velos system by clicking the "Patient Search" tab (from the screen showing patients enrolled in the study – see step 1, on page 7) or by clicking the Patient Search Icon, which is always present at the top of the Velos screen.



11. UM users verify that "University of Michigan" is selected in the "Organization" drop-down box. All users from sites outside UM verify that "Training University" is selected in the "Organization" dropdown box.

In the Velos production database, you will select your actual organization (i.e., your site – University of Michigan, Case Western, etc.) to find a list of registered Velos patients in your organization. For sites outside UM, there will be no patients from your site in the Velos production database until you begin registering them.

Enter/select search criteria in any of the other boxes, then click the "Search" button. (For the purposes of training / certification, enter any search criteria you'd like.) The list of search results can be sorted by clicking the heading of any column; navigate to additional pages of the list by clicking on the arrow buttons above the left-hand side of the list.



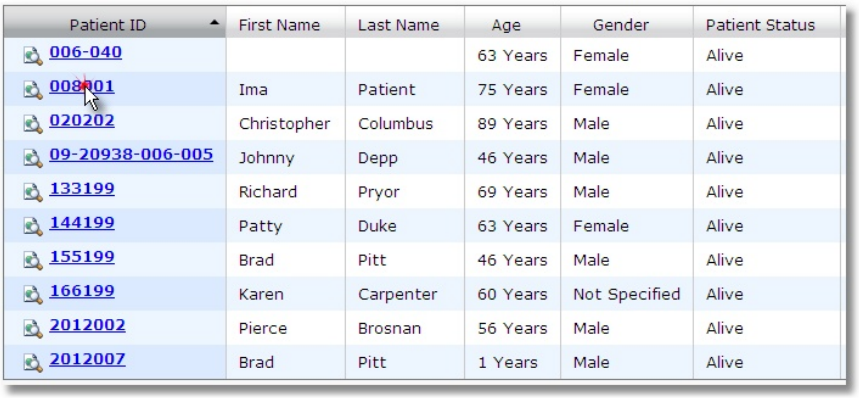
Patient ID	First Name	Last Name	Age	Gender	Patient Status	Other ID(s)	On a Study
006-040			63 Years	Female	Alive	View	Yes (1) AE SCH FORM
008001	Ima	Patient	75 Years	Female	Alive	View	Yes (2) AE SCH FORM
020202	Christopher	Columbus	89 Years	Male	Alive	View	Yes (1) AE SCH FORM
09-20938-006-005	Johnny	Depp	46 Years	Male	Alive	View	Yes (2) AE SCH FORM
133199	Richard	Pryor	69 Years	Male	Alive	View	No AE SCH FORM
144199	Patty	Duke	63 Years	Female	Alive	View	No AE SCH FORM
155199	Brad	Pitt	46 Years	Male	Alive	View	No AE SCH FORM
166199	Karen	Carpenter	60 Years	Not Specified	Alive	View	No AE SCH FORM
2012002	Pierce	Brosnan	56 Years	Male	Alive	View	Yes (1) AE SCH FORM
2012007	Brad	Pitt	1 Years	Male	Alive	View	Yes (2) AE SCH FORM

The Velos "Patient ID" should be a unique number. For patients registered to the University of Michigan organization in the Velos production database, this number is the UMH CPI number. Sometimes this number begins with a leading zero, which must be included in Velos. For sites outside UM, the Velos "Patient ID" is a six-digit number comprised of the site number (see table, below) and an

incremental number for each site, including leading zeros, beginning with 001; e.g., the first patient enrolled at NYUMC would have a Velos Patient ID of 001001; the second patient, 001002; etc.

Site	Site ID
University of Michigan	000
NYUMC	001
Johns-Hopkins	002
Toronto	009
Case Western Reserve University	020
Children's Hospital – LA	021
Harbor – UCLA	022
Long Island Jewish	023
Mayo	024
Montefiore	025
University of Miami	026
University of North Carolina	027
University of Pennsylvania	028
University of Washington	029
NIDDK Intramural	030

12. Verify the Velos Patient ID of the patient you wish to enroll in the study, then click the "Patient ID" link to the left of the patient's name. (For the purposes of training / certification, just select any patient.)

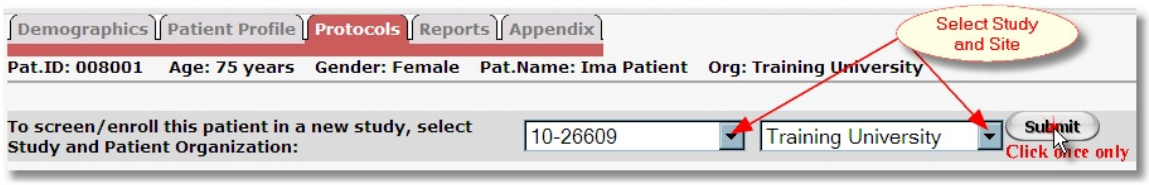


Patient ID	First Name	Last Name	Age	Gender	Patient Status
006-040			63 Years	Female	Alive
008001	Ima	Patient	75 Years	Female	Alive
020202	Christopher	Columbus	89 Years	Male	Alive
09-20938-006-005	Johnny	Depp	46 Years	Male	Alive
133199	Richard	Pryor	69 Years	Male	Alive
144199	Patty	Duke	63 Years	Female	Alive
155199	Brad	Pitt	46 Years	Male	Alive
166199	Karen	Carpenter	60 Years	Not Specified	Alive
2012002	Pierce	Brosnan	56 Years	Male	Alive
2012007	Brad	Pitt	1 Years	Male	Alive

13. Select the NEPTUNE study (study number 10-26609) from the dropdown box and verify that "University of Michigan" (for UM users) or "Training University" (for offsite users) appears in the second dropdown box.

In the Velos production database you will verify that your actual organization (i.e., your site – University of Michigan, Johns-Hopkins, etc.) appears in the second dropdown box.

Click the “Submit” button to begin the study enrollment process.



14. In the "Patient Study Status" window that appears, enter the following mandatory data (designated by red asterisks):

    a. Status – select "Enrolled" from the dropdown box.

    b. Status Date – click the "Select Date" link and select today's date (or whatever date you wish to record as the date the patient was enrolled in the study).

    c. Patient Study ID – defaults to the patient's Velos Patient ID. **Change this number** to match the formula YR-IRB#-Site#-### as follows:

        1) YR = last 2 digits of the current year/year patient enrolled in the study (e.g., 10 for a patient enrolled in 2010, 11 for a patient enrolled in 2011, etc.)

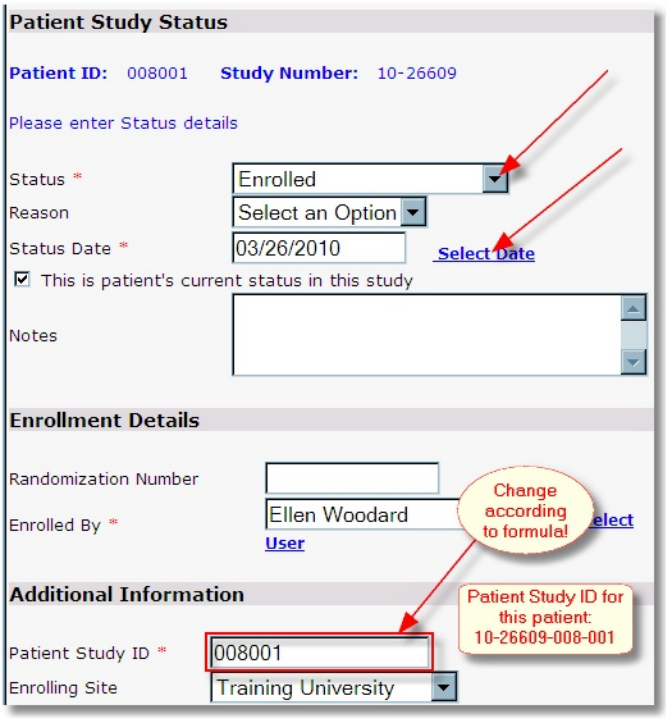
        2) UM's IRB# = 26609

        3) Site# per the following table:

Site	Site ID
University of Michigan	000
NYUMC	001
Johns-Hopkins	002
Toronto	009
Case Western Reserve University	020
Children's Hospital – LA	021
Harbor – UCLA	022
Long Island Jewish	023
Mayo	024
Montefiore	025
University of Miami	026
University of North Carolina	027
University of Pennsylvania	028
University of Washington	029
NIDDK Intramural	030

        4) ### = incremental number for each site, including leading zeros, beginning with 001.

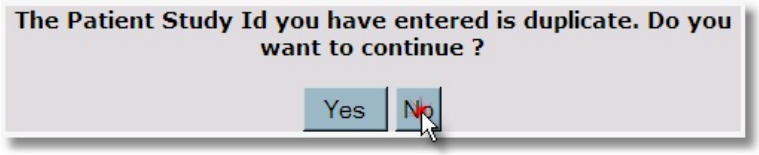
    For example, the first patient enrolled at the UM site would have the Patient Study ID 10-26609-000-001; the second patient enrolled at the UM site would have the Patient Study ID 10-26609-000-002, etc.



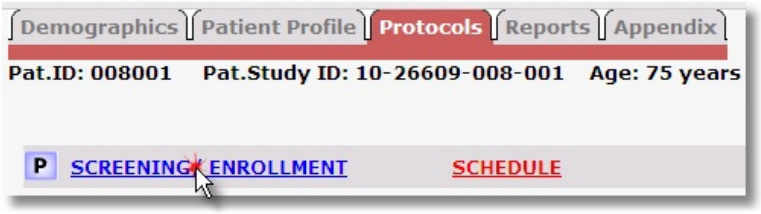
It is not necessary to enter or change any other information in this window.

15. Scroll down to enter your e-Signature and click the "Submit" button.

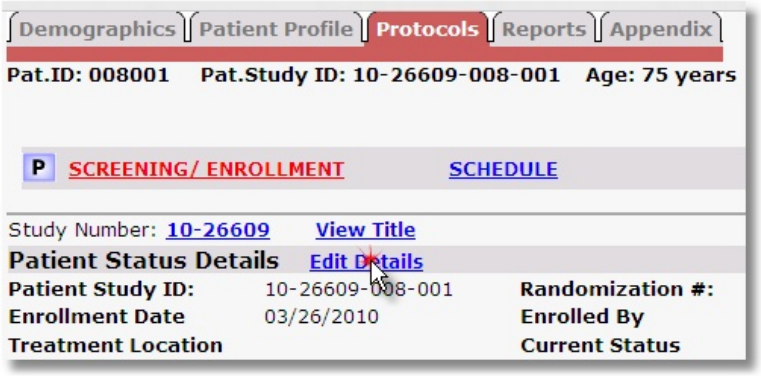
If you entered a duplicate Patient Study ID, an error message will appear. Click "No" (to avoid creation of a duplicate ID) and the Patient Study Status window will reappear. Enter a non-duplicate Patient Study ID, scroll down to enter your e-Signature and click the "Submit" button.



If, for any reason, you find it necessary to return to the "Patient Study Status" window, click the "Screening/Enrollment" link on the "Protocols" tab of the "Manage Patient" section.



Then click the "Edit Details" link next to "Patient Status Details."

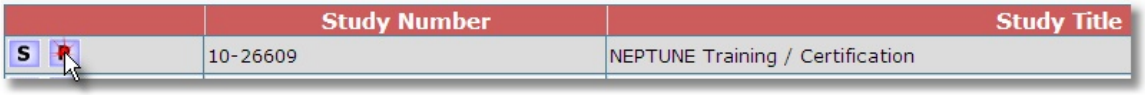


You are now done enrolling an existing patient in the study.

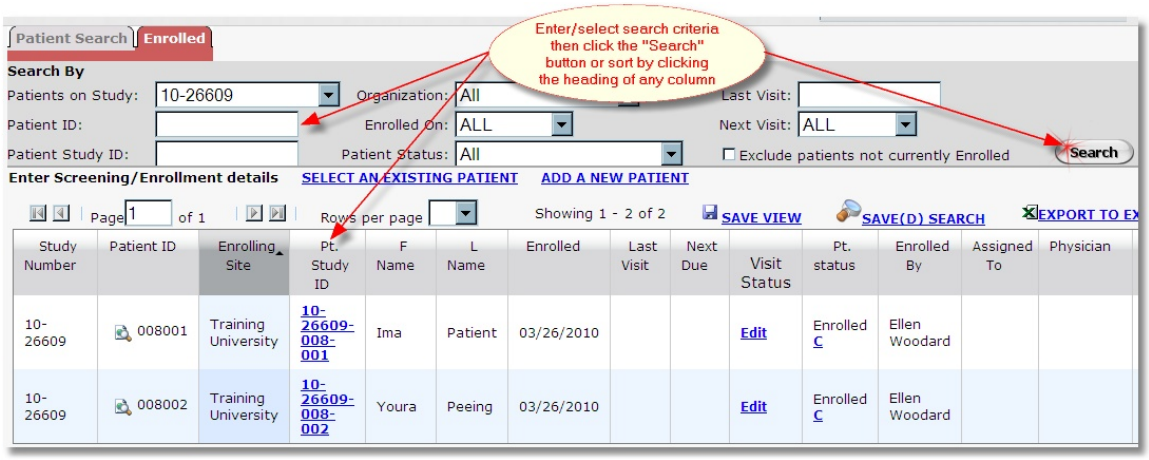
Change a Patient's Status

During the course of the study, it may become necessary to change a patient's status from "Enrolled" to "Off Study" for any number of reasons (e.g., death, lost to follow-up, etc.). For the purposes of training / certification, please change the status of one of the patients you enrolled.

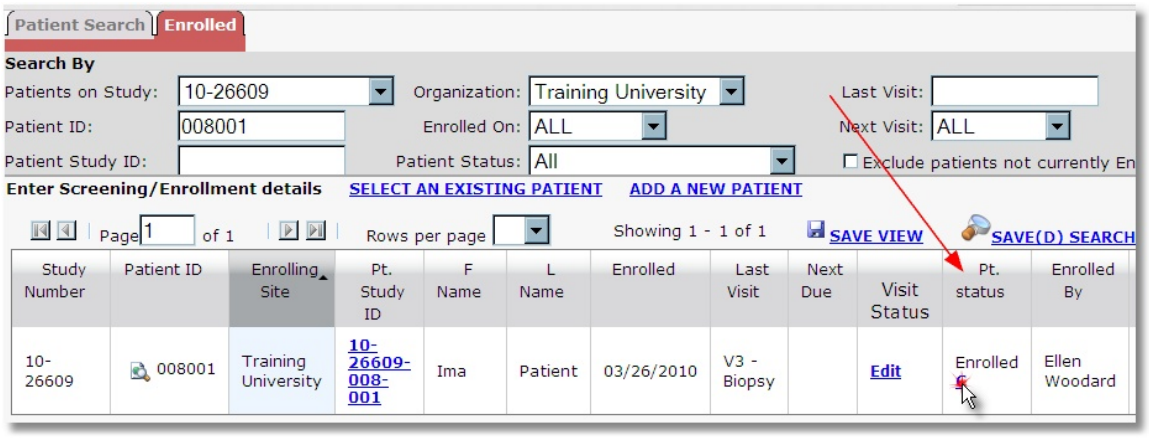
16. From your Homepage, click the "P" icon to the left of the NEPTUNE study (study number 10-26609) to go to the list of patients enrolled in the study.



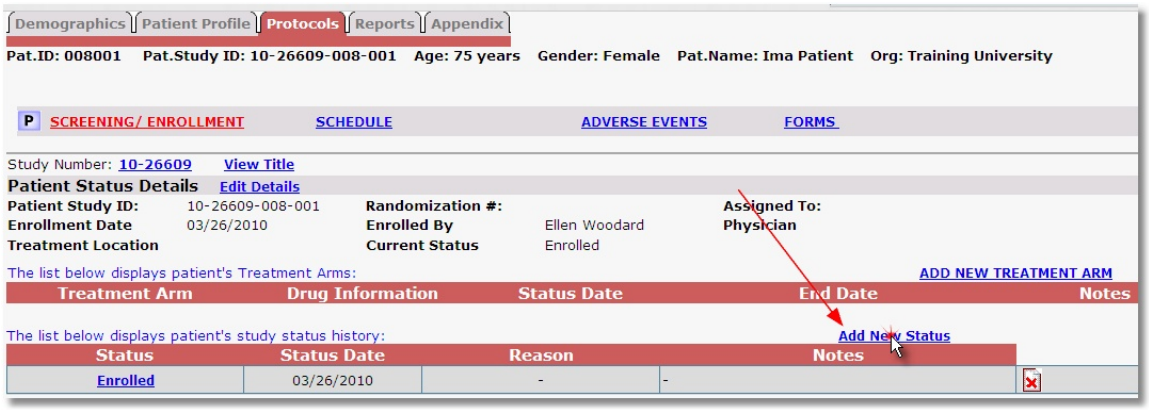
To find your patient, the list of enrolled patients can be sorted by clicking the heading of any column; navigate to additional pages of the list by clicking the arrow button above the left-hand side of the list. You can also enter/select search criteria in any of the boxes, then click the "Search" button.



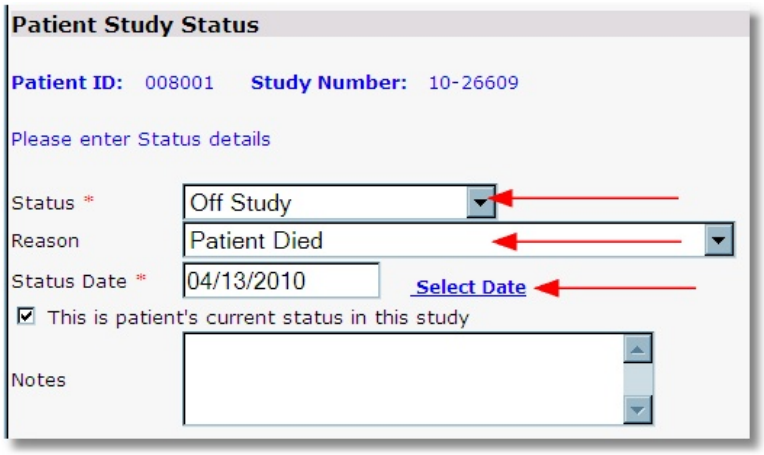
17. Click the "C" link in the "Pt. Status" column of the patient whose status you need to change.



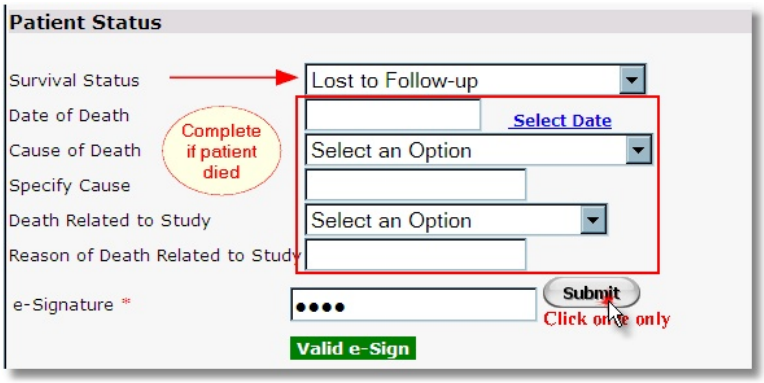
18. Click the "Add New Status" link.



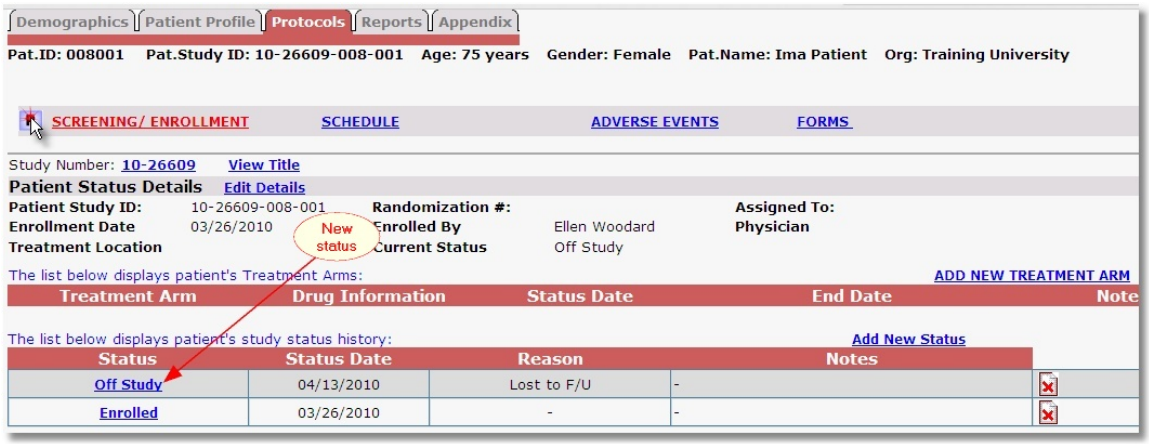
19. In the "Patient Study Status" section of the window that appears, select "Off Study" from the "Status" dropdown box, select the appropriate reason from the "Reason" dropdown box (e.g., "Patient Died", "Lost to F/U", etc.), then click the "Select Date" link to select the "Status Date" from the calendar.



20. Scroll down to the "Patient Status" section and select the patients "Survival Status" from the dropdown box. If the patient died, complete the additional information related to death, enter your e-Signature and click the "Submit" button.



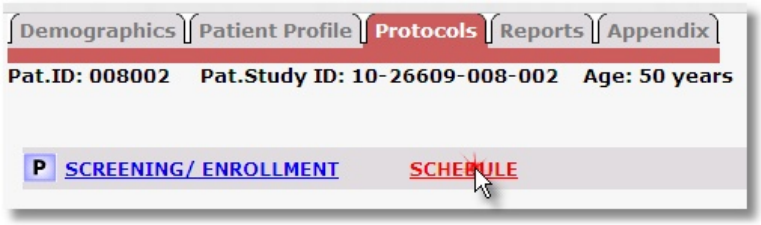
21. Note the addition of the new status in the status list.



Click on the "P" icon near the upper left-hand side of the screen and note the change of the patient's status in the list of patients enrolled in the study.

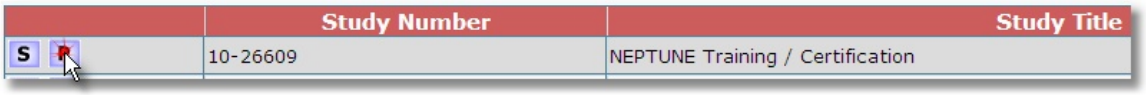
C. Link your enrolled patients to the NEPTUNE study calendar

1. If you have just finished enrolling an existing or new patient in the study and are on the "Protocols" tab of the "Manage Patient" section, click the "Schedule" link.

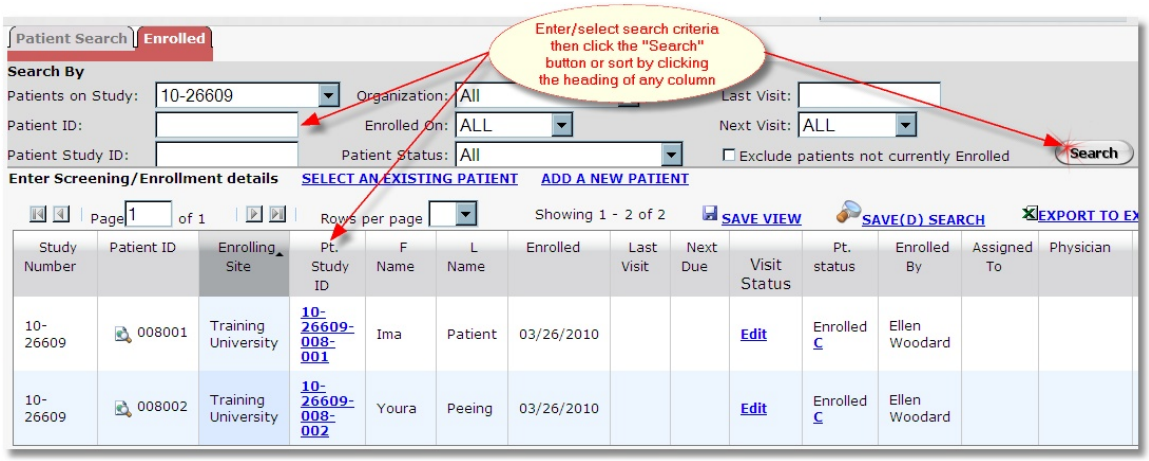


or

From your Homepage, click the "P" icon to the left of the NEPTUNE study (study number 10-26609) to go to the list of patients enrolled in the study.

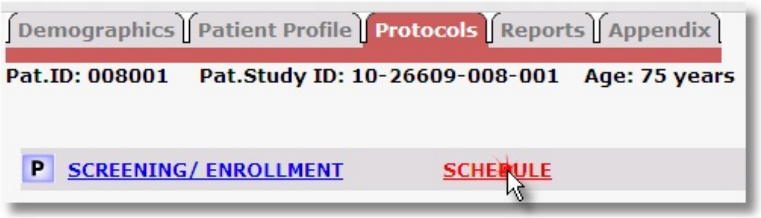


To find your patient, the list of enrolled patients can be sorted by clicking the heading of any column; navigate to additional pages of the list by clicking the arrow button above the left-hand side of the list. You can also enter/select search criteria in any of the boxes, then click the "Search" button.



Click the "Pt. Study ID" link to the left of the patient's name.

Then click the “Schedule” link.

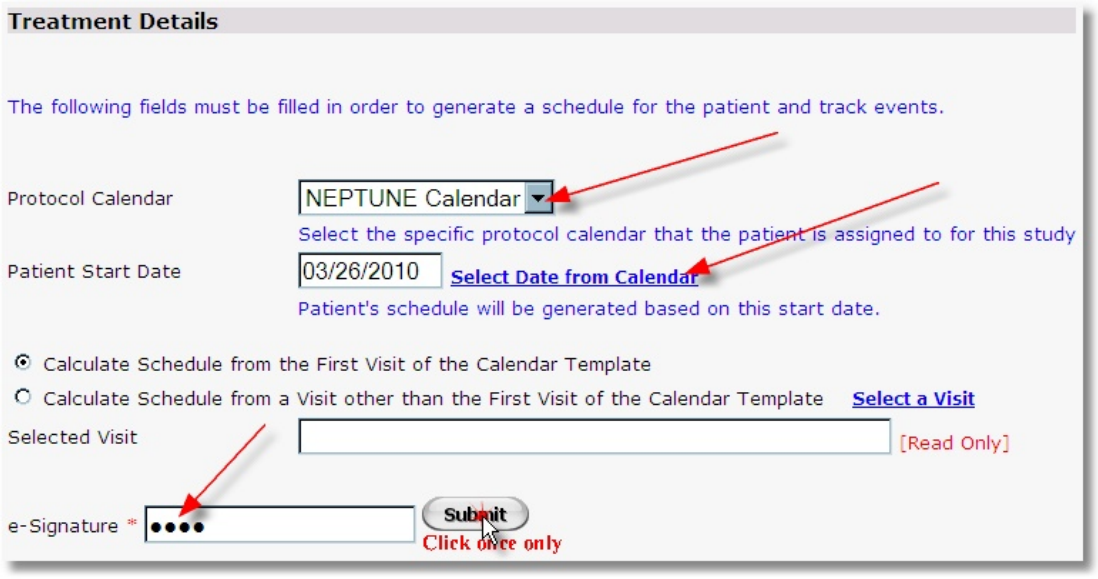


2. Click the "Edit Calendar/Date" link.

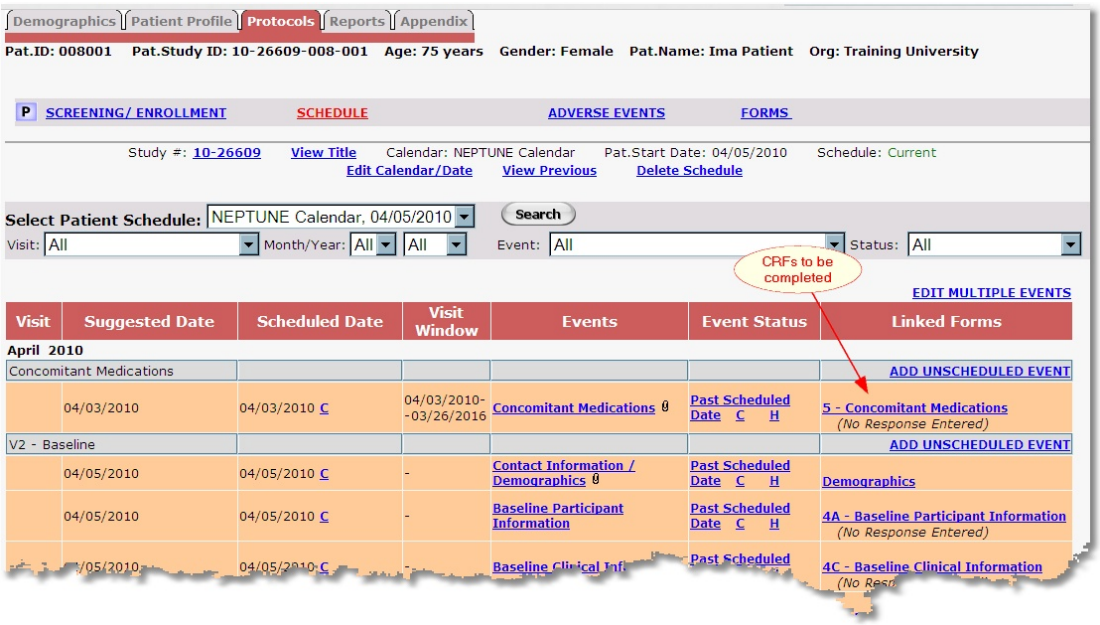
a. Select the NEPTUNE Calendar from the "Protocol Calendar" dropdown box.

b. Click the "Select Date from Calendar" link to select the patient's start date. Select today's date or whatever date you wish to record as the start of the patient's schedule.

c. Enter your e-Signature and click the "Submit" button.



Note that the patient's study schedule appears. CRFs to be completed are listed in the right-hand column ("Linked Forms") of the schedule. You will be guided through actual completion of the CRFs later, in Section D. Please continue with "Add an Unscheduled Event", below.



Add an Unscheduled Event

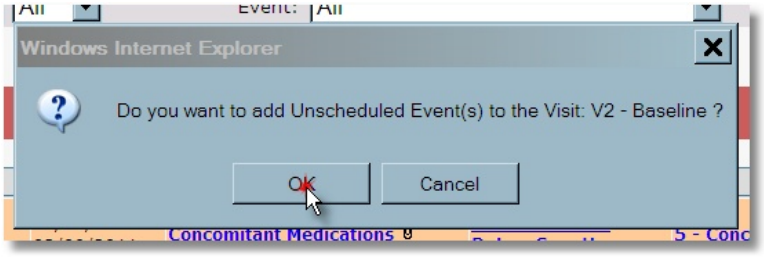
Appropriate quality of life surveys are added to the patient's calendar via an "Unscheduled Event" with corresponding, age-appropriate CRF(s) for data entry. Additionally, if a patient experiences an adverse event or receives a follow-up, surveillance or other diagnostic renal biopsy at any time during the study an "Unscheduled Event" is added to the calendar with a corresponding CRF for data entry. For the purposes of training / certification, you will add an age-appropriate

Quality of Life Survey event to the "V2 – Baseline" visit and an Adverse Event event to the "V3 – Biopsy" visit. (Adding an unscheduled event for an additional renal biopsy would be accomplished in the same way as adding an Adverse Event.)

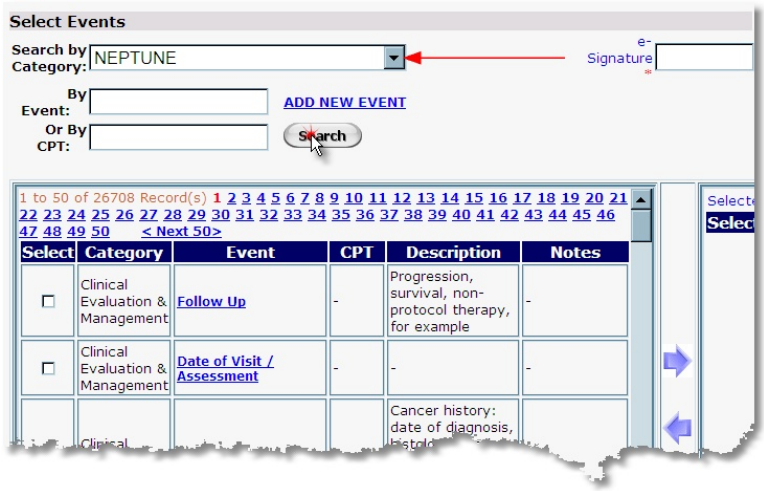
3. To add an age-appropriate Quality of Life Survey event, click on the "Add Unscheduled Event" link to the right of visit "V2 – Baseline".

In the Velos production database, the Quality of Life Survey event will be added to whichever visit is currently being conducted; i.e., V2, V4, V6, V8, etc.

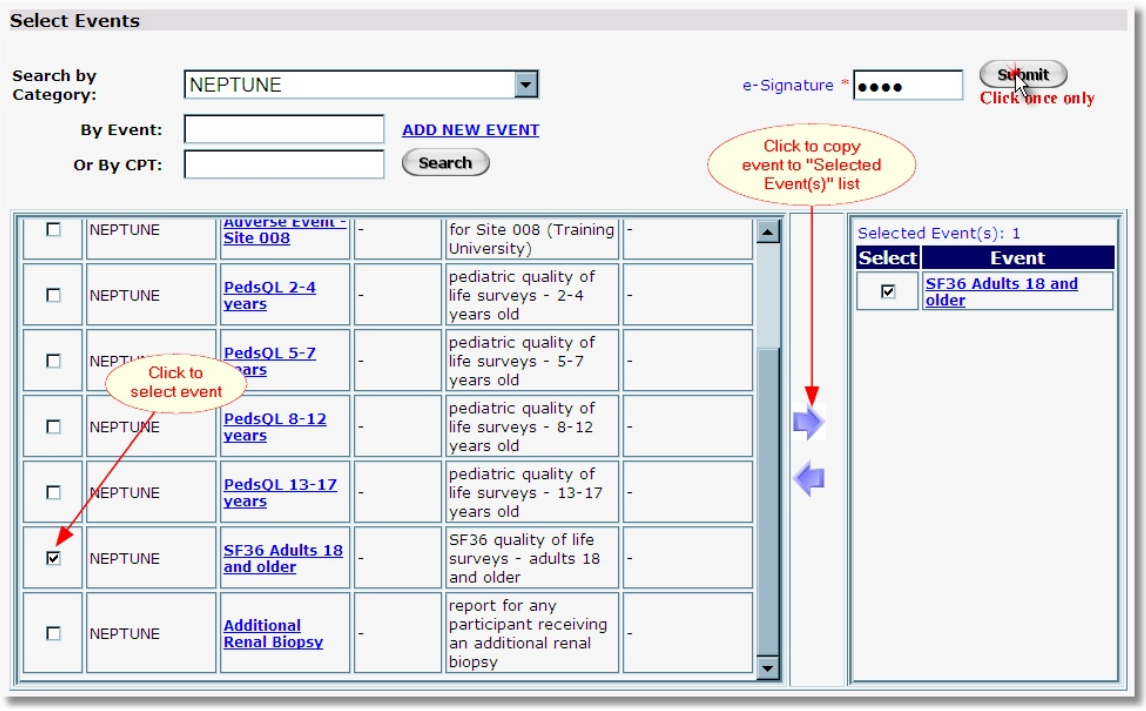
4. Click the "OK" button to confirm you want to add an unscheduled event to the "V2 – Baseline" visit.



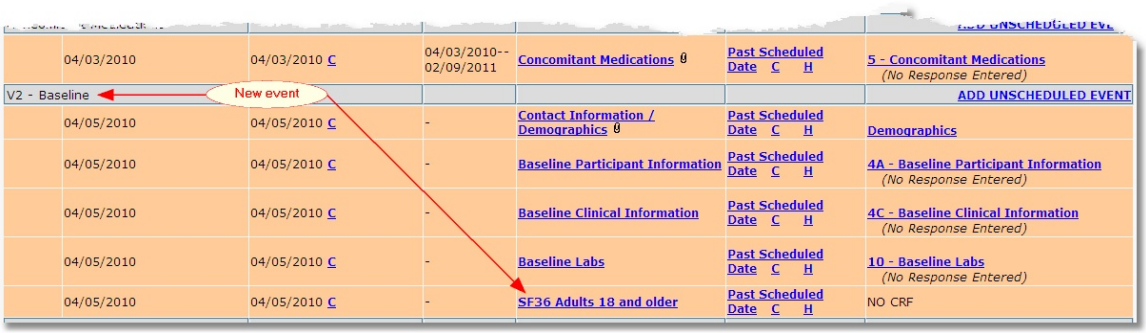
5. In the "Select Events" window that appears, select "NEPTUNE" from the "Search by Category" dropdown box, then click the "Search" button.



6. Note the age of your patient and click to select the checkbox to the left of the age-appropriate Quality of Life Survey event. Click the right-arrow to copy the event to the "Selected Event(s)" list, then enter your e-Signature and click the "Submit" button.

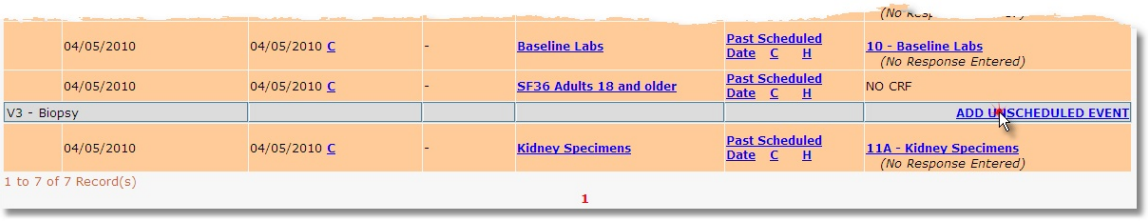


Note that the event now shows up under the "V2 – Baseline" visit.



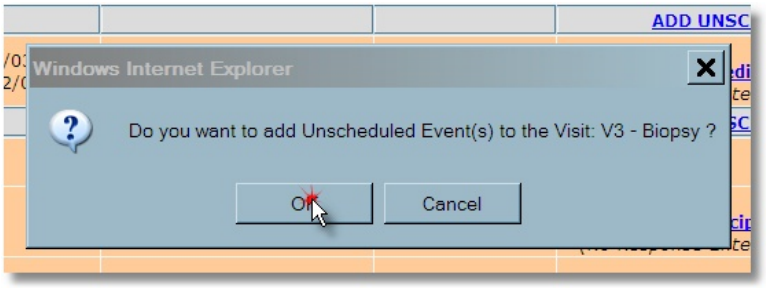
For the purposes of training / certification, no CRF(s) have been attached to the Quality of Life Survey events. In the Velos production database, one or two CRFs will appear in the "Linked Forms" column, depending on the age range selected.

7. To add an Adverse Event event, scroll down to the "V3 – Biopsy" visit and click on the "Add Unscheduled Event" link to the right of the visit name.

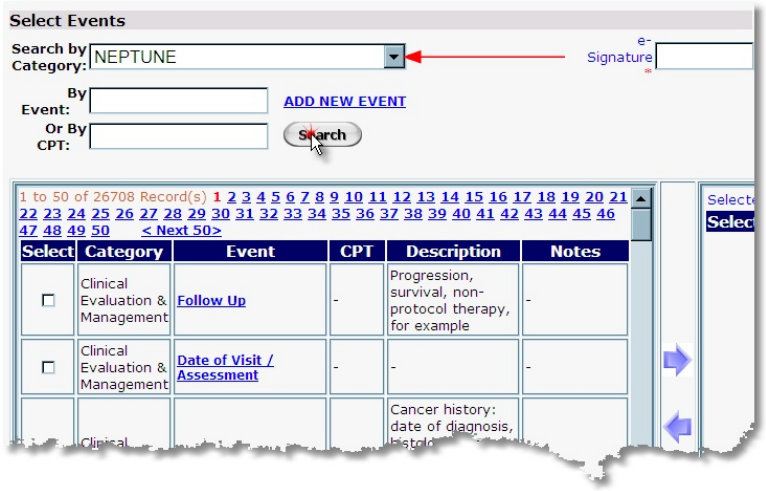


In the Velos production database, the Adverse Event event will be added to the visit closest to when the adverse event occurred.

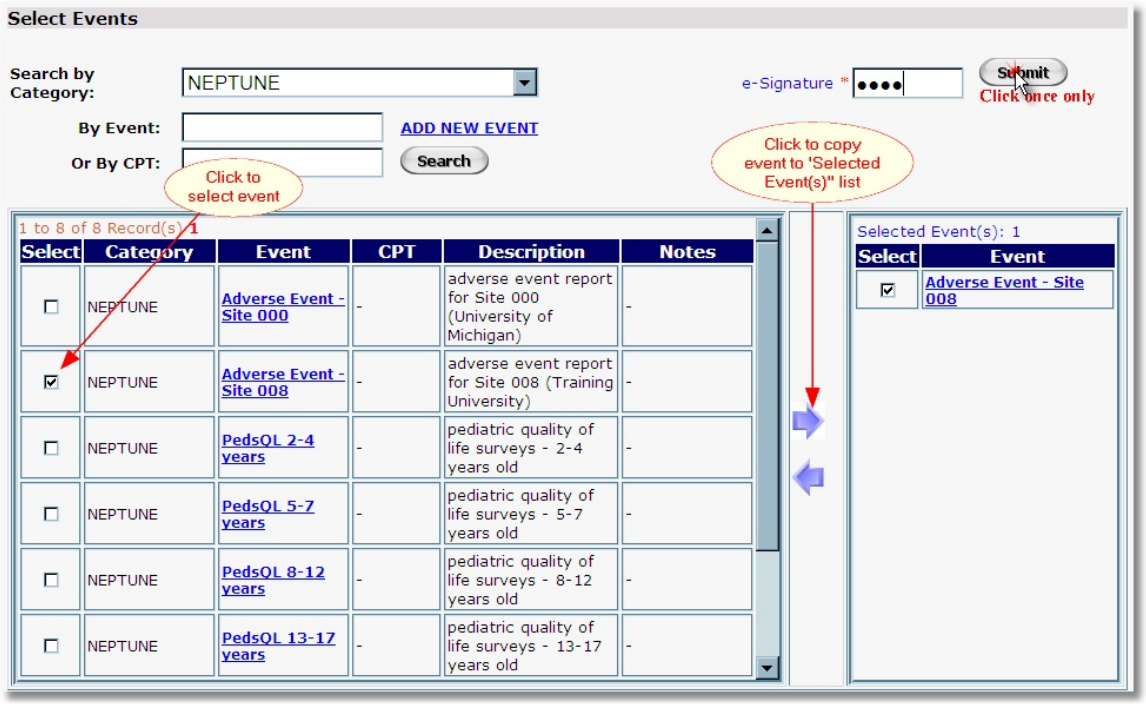
8. Click the "OK" button to confirm you want to add an unscheduled event to the "V3 – Biopsy" visit.



9. In the "Select Events" window that appears, select "NEPTUNE" from the "Search by Category" dropdown box, then click the "Search" button.

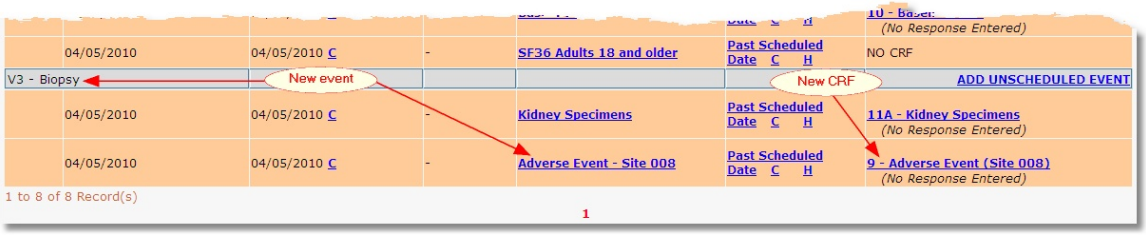


10. Click to select the checkbox to the left of Adverse Event event for your site (Site 000 for UM; Site 008 for sites outside UM). Click the right-arrow to copy the event to the "Selected Event(s)" list, then enter your e-Signature and click the "Submit" button.



In the Velos production database, you will select the Adverse Event event for your site; e.g., Site 022 for Harbor – UCLA, Site 023 for Long Island Jewish, etc..

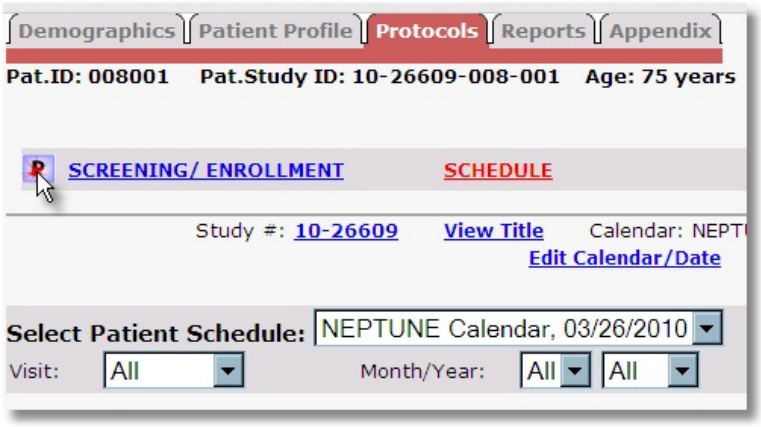
Note that the "Adverse Event" event (with associated CRF) now shows up under the "V3 – Biopsy" visit.



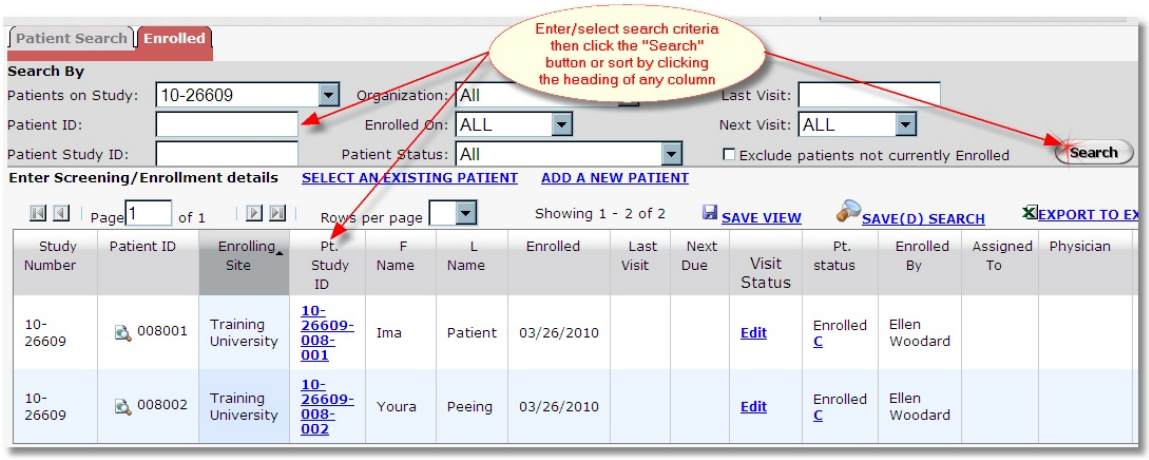
You are now done linking your patient to the study calendar and adding unscheduled events.

Continue with the next step to link your next patient to the study calendar or if you have already linked all your patients to the study calendar, skip to section D, below.

11. Click the "P" icon near the upper left of the screen to return to the list of patients enrolled in the study.

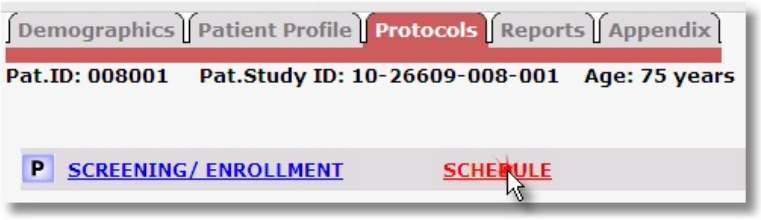


To find your next patient, the list of enrolled patients can be sorted by clicking the heading of any column; navigate to additional pages of the list by clicking the arrow button above the left-hand side of the list. You can also enter/select search criteria in any of the boxes, then click the "Search" button.



12. Click the "Pt. Study ID" link to the left of the next patient's name.

Then click the “Schedule” link and repeat above steps (beginning with step 2, on page 21) to link the next patient to the study calendar.

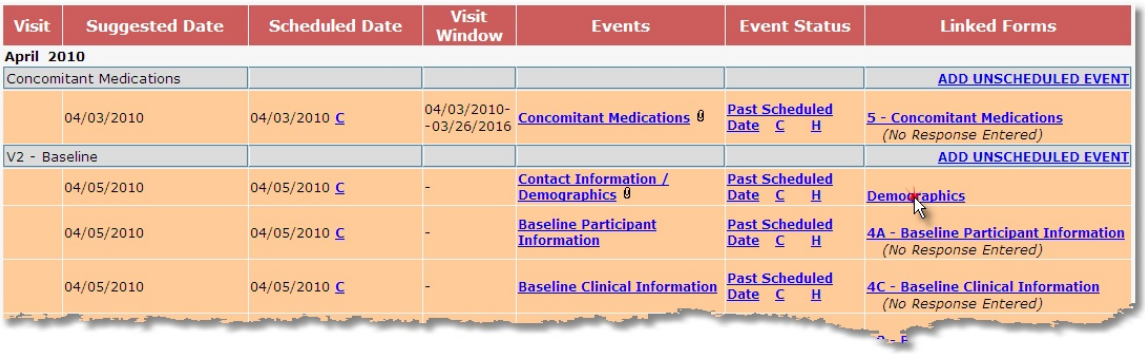


D. Enter Demographic and CRF data for your patients enrolled in the NEPTUNE study

(Refer to the Patient "Dummy" History, *beginning on page 40*, and the Patient "Dummy" Histology Report, attached separately as a plain text file, for data to complete the NEPTUNE Certification CRFs)

Enter Demographics Information

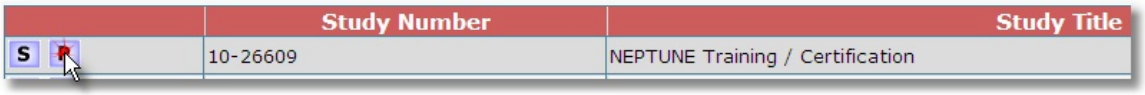
1. If you have just finished linking a patient to the study calendar and are on the "Protocols" tab of the "Manage Patient" section with the patient's schedule showing, click the "Demographics" link in the "Linked Forms" column under visit "V2 – Baseline" of the patient's schedule.



Visit	Suggested Date	Scheduled Date	Visit Window	Events	Event Status	Linked Forms
April 2010						
Concomitant Medications						ADD UNSCHEDULED EVENT
	04/03/2010	04/03/2010 C	04/03/2010- -03/26/2016	Concomitant Medications	Past Scheduled Date C H	5 - Concomitant Medications (No Response Entered)
V2 - Baseline						ADD UNSCHEDULED EVENT
	04/05/2010	04/05/2010 C	-	Contact Information / Demographics	Past Scheduled Date C H	Demographics
	04/05/2010	04/05/2010 C	-	Baseline Participant Information	Past Scheduled Date C H	4A - Baseline Participant Information (No Response Entered)
	04/05/2010	04/05/2010 C	-	Baseline Clinical Information	Past Scheduled Date C H	4C - Baseline Clinical Information (No Response Entered)

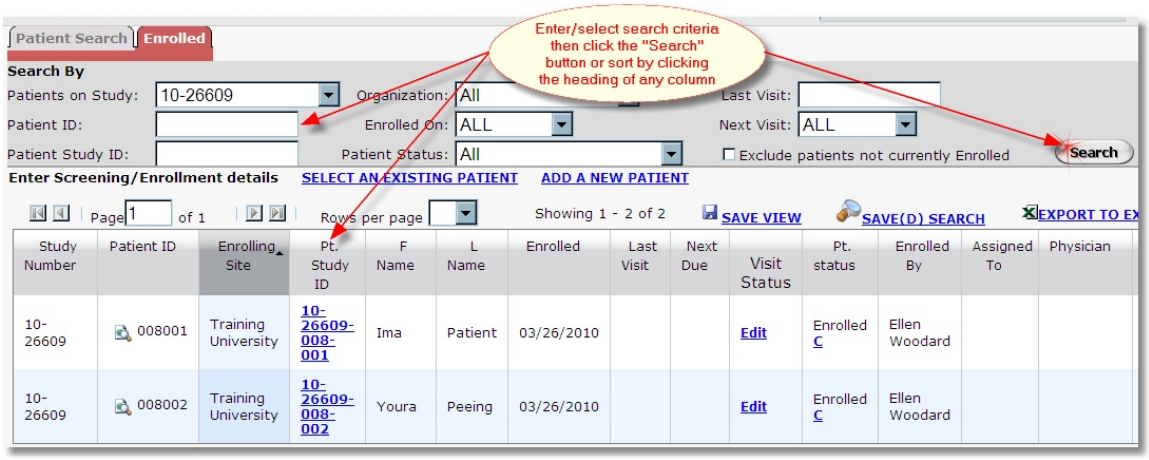
or

From your Homepage, click the "P" icon to the left of the NEPTUNE study (study number 10-26609) to go to the list of patients enrolled in the study.



	Study Number	Study Title
S P	10-26609	NEPTUNE Training / Certification

To find your patient, the list of enrolled patients can be sorted by clicking the heading of any column; navigate to additional pages of the list by clicking the arrow button above the left-hand side of the list. You can also enter/select search criteria in any of the boxes, then click the "Search" button.

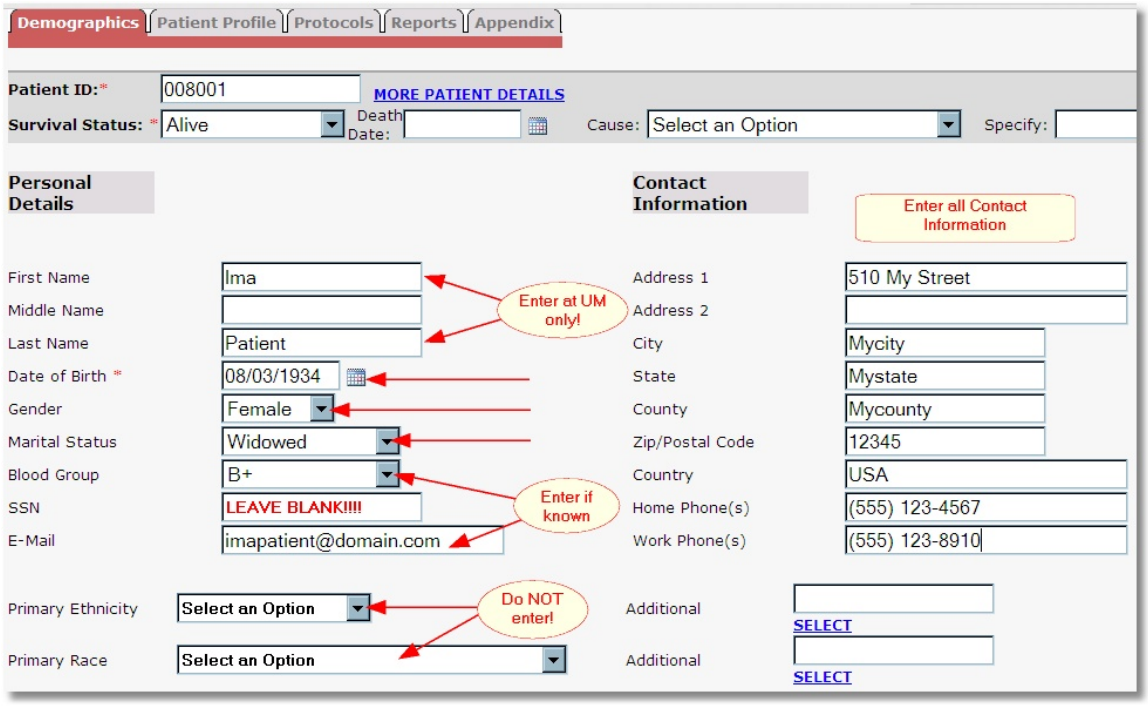


Click the "Pt. Study ID" link to the left of the patient's name.

Then click the "Demographics" link in the "Linked Forms" column under visit "V2 – Baseline" of the patient's schedule.

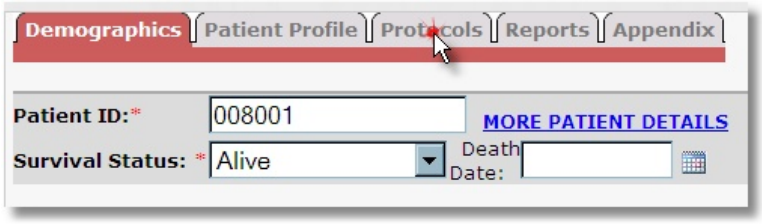
2. In the Demographics window, enter and/or verify (if it's already there) the following data (for the purposes of training / certification, you can make up this information):
   a. Date of Birth – click the calendar icon to select the date
   b. Gender – select from the dropdown box
   c. Marital Status – select from the dropdown box
   d. Blood Group – if known, select from the dropdown box
   e. E-Mail – if known, enter
   f. Contact Information – enter all

*To protect external site PHI, enter First Name and Last Name in this window at **UM only**.*
*SSN (Social Security Number) is **NOT** to be entered in Velos.*
*Do **NOT** enter Primary Ethnicity and/or Race in this window – this data is collected elsewhere.*



3. Scroll down to enter your e-Signature and click the "Submit" button.

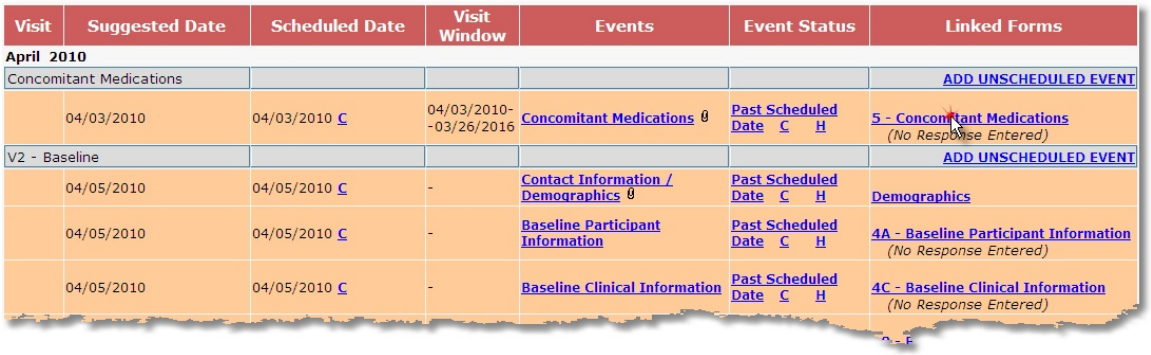
4. Click on the "Protocols" tab:



Then click on the Study Number link (10-26609) to the left of the NEPTUNE Training / Certification study.

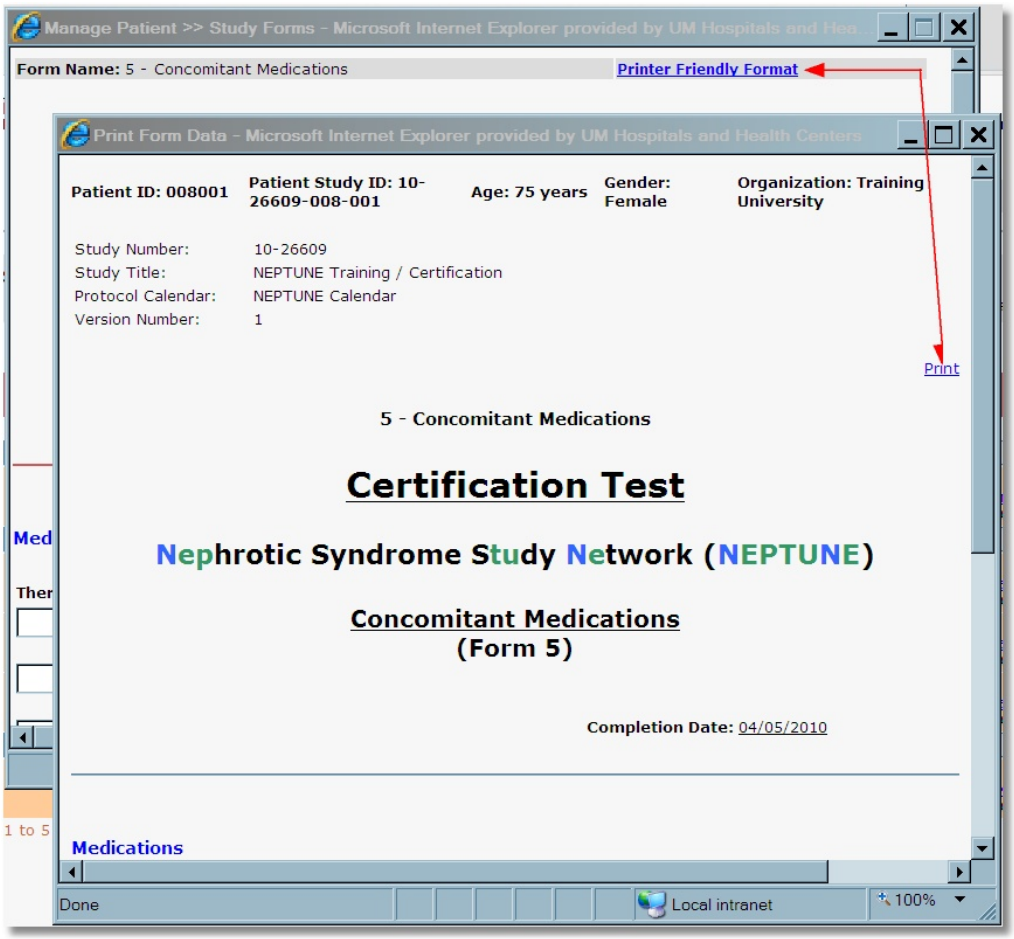
Enter CRF Data

5. CRFs to be completed are listed in the "Linked Forms" (right-hand) column of the patient schedule. Click on the name of a CRF to open it.



Visit	Suggested Date	Scheduled Date	Visit Window	Events	Event Status	Linked Forms
April 2010						
Concomitant Medications						ADD UNSCHEDULED EVENT
	04/03/2010	04/03/2010 C	04/03/2010--03/26/2016	Concomitant Medications	Past Scheduled Date C H	5 - Concomitant Medications (No Response Entered)
V2 - Baseline						ADD UNSCHEDULED EVENT
	04/05/2010	04/05/2010 C	-	Contact Information / Demographics	Past Scheduled Date C H	Demographics
	04/05/2010	04/05/2010 C	-	Baseline Participant Information	Past Scheduled Date C H	4A - Baseline Participant Information (No Response Entered)
	04/05/2010	04/05/2010 C	-	Baseline Clinical Information	Past Scheduled Date C H	4C - Baseline Clinical Information (No Response Entered)

You can print a CRF by clicking the "Printer Friendly Format" link at the top of the CRF window, then clicking the "Print" link near the top, right of the "Print Form Data" window. This can be useful for printing a completed CRF to verify data entry.



6. Enter data in the CRF as follows:
   a. Completion Date – leave as the default (which is today).
   b. Enter the remainder of the CRF information using the Patient "Dummy" History, beginning on page 40 and the Patient "Dummy" Histology Report, attached as a separate, plain text file.

7. At the bottom of the CRF, select the appropriate status of your data entry in the "Form Status" dropdown box as follows
   a. "Completed" indicates you are done entering data
   b. "Work in Progress" indicates you need to come back to the CRF to enter additional data.

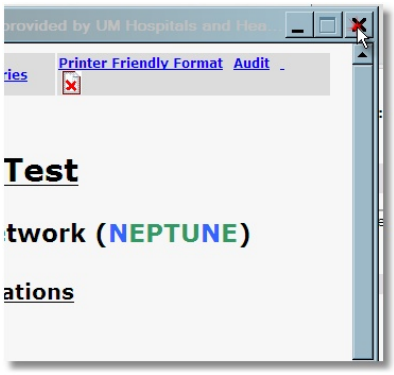
8. Enter your e-Signature and click the "Submit" button.

9. A message window appears asking if you want to mark this event in the "Event Status" column on the patient's schedule as "Done."

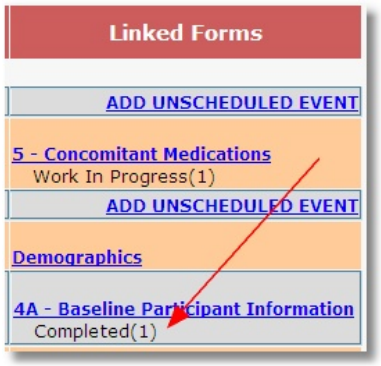
   If **yes** (i.e., you are done entering data in the CRF and selected a "Form Status" of "Completed"), continue with the next step (a). If **no** (i.e., you selected a "Form Status" of "Work In Progress" because you need to come back to this CRF and enter additional data), skip step a and go to step b:

   a. If you selected a "Form Status" of "Completed" and want to mark this event as "Done," enter your e-Signature and click "Submit."

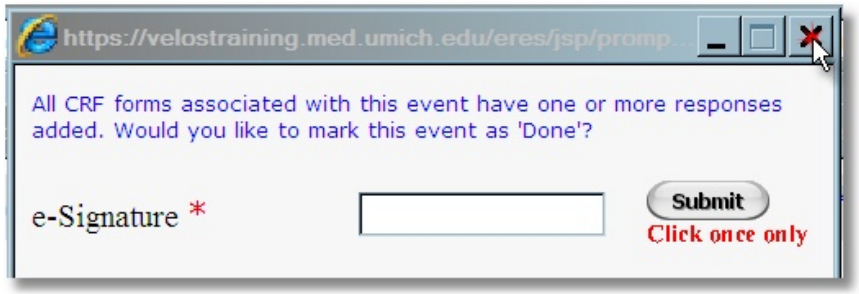
   Click the "X" in the upper right-hand corner of the CRF window to close it and return to the patient schedule.



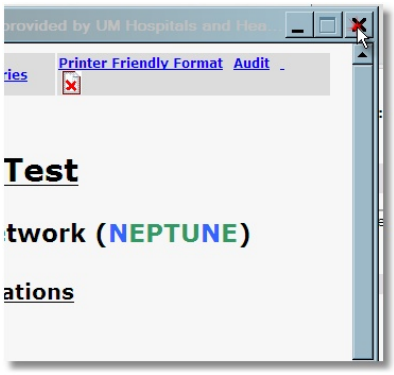
Note that the CRF is now listed as "Completed" on the patient schedule.



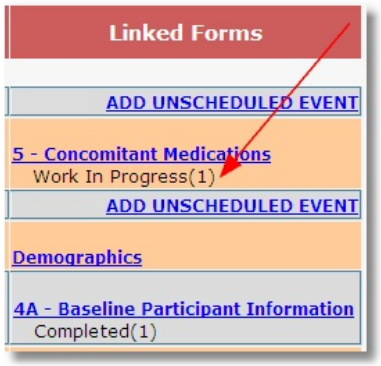
b. If you selected a form status of "Work in Progress" because you need to come back to this CRF to enter additional data or it is otherwise incomplete, **DO NOT** enter your e-Signature. Click the "X" in the upper right-hand corner of the message window to close it.



Click the "X" in the upper right-hand corner of the CRF window to close it and return to the patient schedule.



Note that the CRF is now listed as "Work In Progress" on the patient schedule.

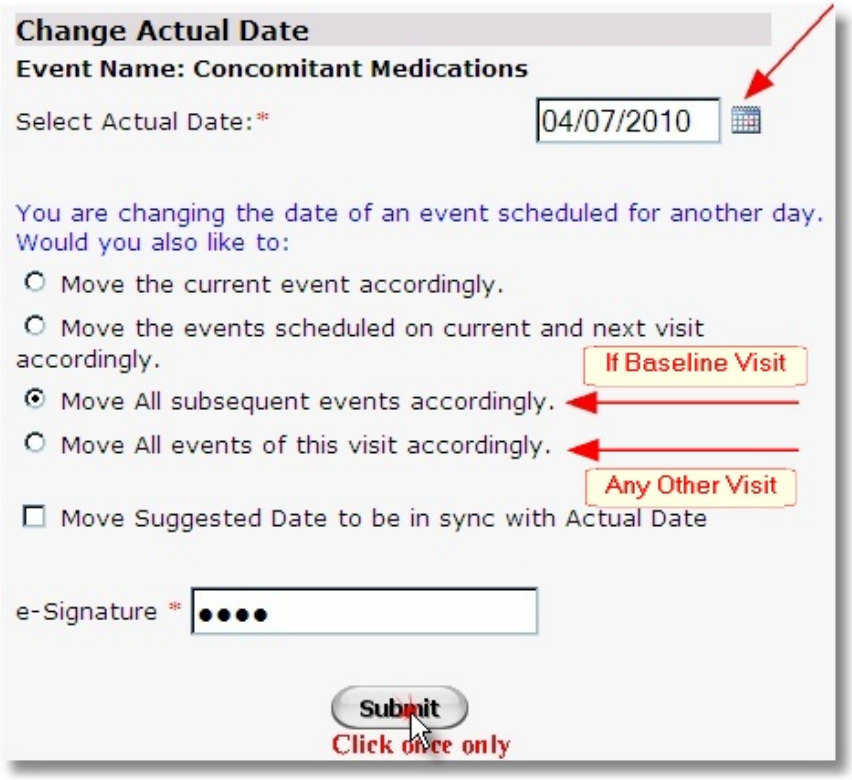


10. Change the Scheduled Date of this event (if the actual date is different from the date listed in the "Scheduled Date" column) by clicking the "C" link next to the date in the "Scheduled Date" column of the patient schedule. If necessary, you can also change the Status of this event by clicking the "C" link in the "Event Status" column of the patient schedule.

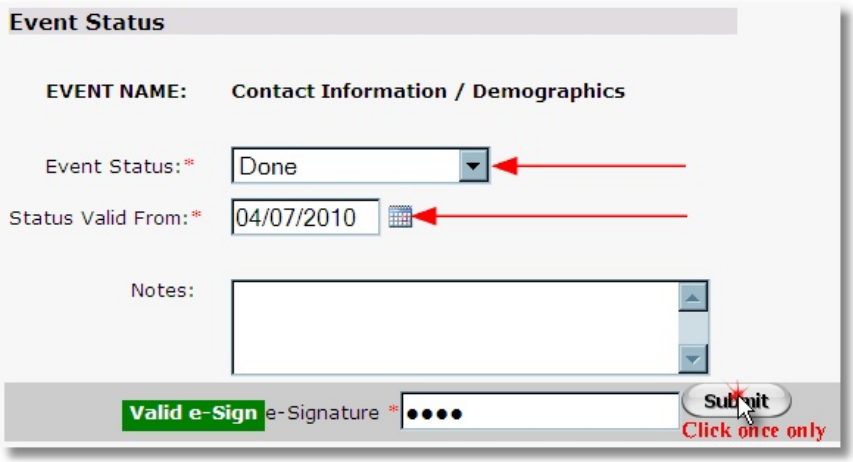
To keep an accurate, ongoing record of when visits occur, always change the "Scheduled Date" to the actual visit date when you complete CRFs. An example of when you would want to change the "Event Status" would include when you've completed entry of Demographics information as this status will not automatically update to "Done."

a. After clicking on the "C" link next to the date in the "Scheduled Date" column of the patient schedule, click the calendar icon to select the actual date and if this is the Baseline visit, click on the "Move All subsequent events accordingly" radio button to reschedule remaining visits and events based on this actual date (since all visits are

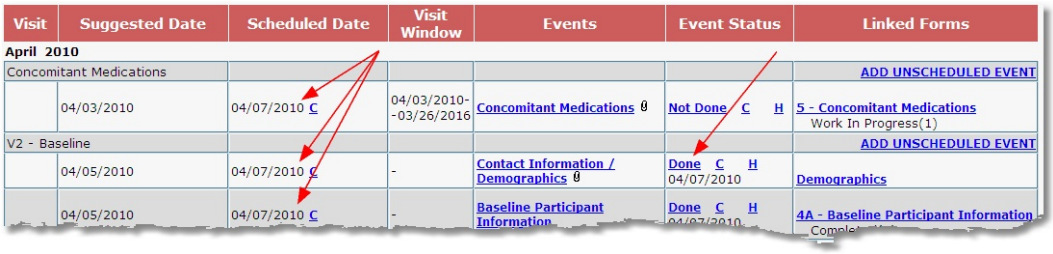
scheduled according to the Baseline visit). For any visit other than Baseline, click on the "Move all events of this visit accordingly" radio button. Enter your e-Signature and click the "Submit" button.



b. After clicking on the "C" link in the "Event Status" column of the patient schedule, select the Event Status from the dropdown box and click the calendar icon to select the date from which this status is valid. Enter your e-Signature and click the "Submit" button.



Note the "Scheduled Date" and "Event Status" have been updated accordingly.



11. Go back to step 5, beginning on page 31, to complete the next CRF or if all CRFs are complete, continue with the next step.

    For training / certification purposes, the following CRFs are to be completed:

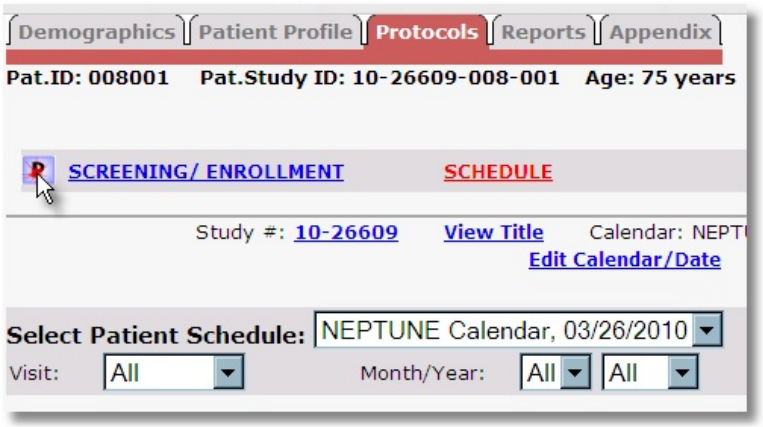
    4A – Baseline Participant Information
    4C – Baseline Clinical Information
    5 – Concomitant Medications
    10 – Baseline Labs
    11A – Kidney Specimens

    Additionally, the following CRF is to be opened, the form status (at the bottom of the CRF) set to "Completed" and saved (enter your e-Signature and click the "Submit" button).

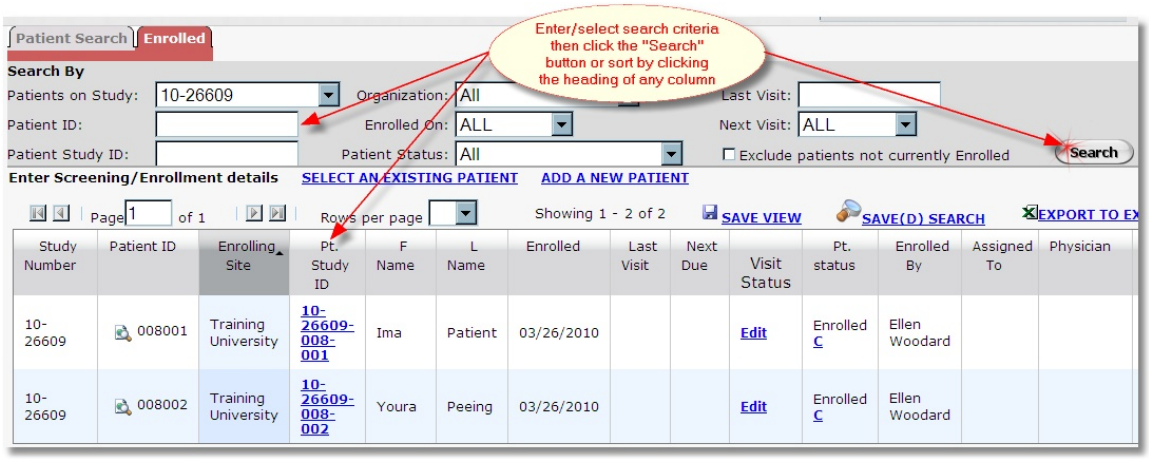
    9 – Adverse Event (Site ###)

    For training / certification purposes, you are required to enter CRF data for only one of the patients you enrolled. If you'd like additional practice with this activity, continue with the next step; otherwise, you have completed the NEPTUNE Hands-on Homework / Certification Test.

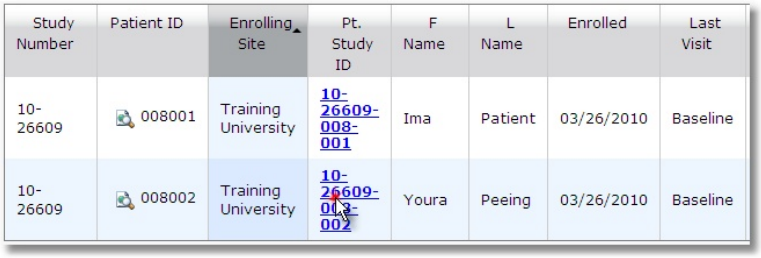
12. Click the "P" icon near the upper left of the screen to return to the list of patients enrolled in the study.



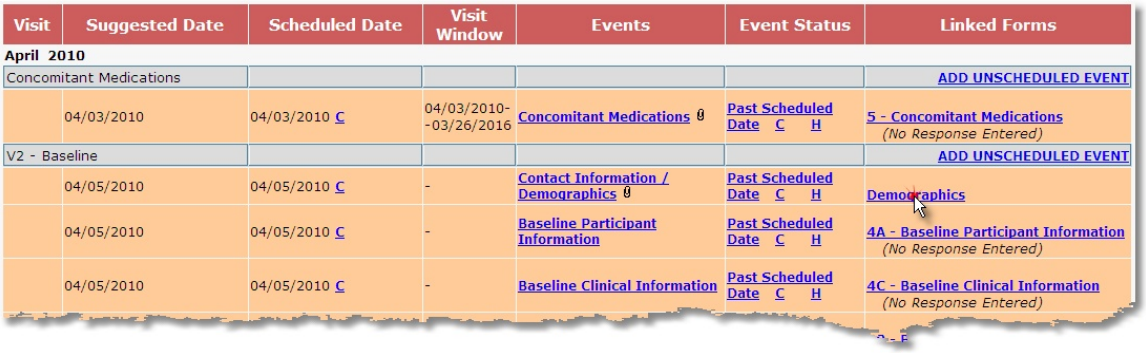
    To find your next patient, the list of enrolled patients can be sorted by clicking the heading of any column; navigate to additional pages of the list by clicking the arrow button above the left-hand side of the list. You can also enter/select search criteria in any of the boxes, then click the "Search" button.



13. Click the "Pt. Study ID" link to the left of the next patient's name.



Then click the "Demographics" link in the "Linked Forms" column under visit "V2 – Baseline" of the patient's schedule.



14. Repeat above steps (beginning with step 2, on page 29) to complete CRFs for the rest of your patients.

END of Hands-on Homework / Certification Test

Complete the Check List on the next page to ensure you've covered all the Hands-on Homework / Certification Requirements.

NEPTUNE Hands-on Homework / Certification Test

Check List

Enrolled 3 patients (2 new, 1 existing)

1. Enrolled 2 new patients (pg. 8) ☐
2. Enrolled 1 existing patient (pg. 13) ☐
3. Entered correct patient IDs for all 3 patients (new – pg. 9; existing – pg. 13) ☐
4. Entered correct patient **study** IDs for all 3 patients (new – pg. 10; existing – pg. 15) ☐
5. Changed at least 1 patient's status (pg. 17) ☐

Linked patients to the study calendar

1. Linked all 3 enrolled patients to the study calendar (pg. 20) ☐
2. Added unscheduled events to all 3 patient calendars (pg. 22) ☐

Entered demographic and CRF data for at least 1 enrolled patient

1. Demographics (pg. 28) ☐
2. 4A – Baseline Participant Information (pg. 31) ☐
3. 4C – Baseline Clinical Information (pg. 31) ☐
4. 5 – Concomitant Medications (pg. 31) ☐
5. 10 – Baseline Labs (pg. 31) ☐
6. 11A – Kidney Specimens (pg. 31) ☐
7. 9 – Adverse Event (Site ###) – opened and marked as "Completed" only (pg. 36) ☐
8. Changed the Scheduled Date of at least one event (pg. 34) ☐
9. Changed the Event Status of at least one event (pg. 35) ☐

Complete the NEPTUNE Velos Training Completion Record, on page 5, and fax to the NEPTUNE Study Office.

Glossary of Terms

Completion Date – On a CRF, the date you entered data into the CRF.

e-Signature – Your personal identification code entered at all points of data entry or change. Provides the means for tracking who enters and changes data.

Form Status – The status of data entry on a CRF (e.g., "Work in Progress" or "Completed").

Organization – Synonymous with "Site" (e.g., University of Michigan, University of Pennsylvania, etc.)

Patient – Synonymous with "Participant" or "Study Participant."

Patient ID – The overall, unique Velos ID assigned to a patient.

Patient Study ID – The unique study ID assigned to a patient. (A patient is entered into Velos only once, so has one Patient ID, but can be involved in more than one study, so can have more than one Patient Study ID.)

Patient-centric database – A unique patient and associated demographics data is entered into the database only once.

Protocol – Synonymous with "Study."

Scheduled Date – Synonymous with "Actual Date."

Velos Production database – The "real" database where actual patients and data are entered.

Velos Training database – A database of "dummy" patients and data used for testing, practicing and training.

Nephrology Clinic Note
Date of Service: 9-04-2010

Eura Peeing M.D.
1776 Liberty Drive, Suite 16
Bubbling Streams, MI, 55555

HPI:
I had the pleasure of seeing, Ms. Ima Payshint, in Nephrology Clinic on September 04, 2010. As you know, she is a 56-year-old African-American female with a history of hypertension, obesity and I am seeing in Nephrology for proteinuria which has been present for several months. She is scheduled to have a kidney biopsy to investigate the cause of her proteinuria. She has been feeling well and has no major complaints and no recent hospitalizations. She denies fever chills, rashes, N/V/D and no recent infections. She has felt fatigue but has no SOB or chest pain. She does admit to occasional leg swelling and foamy urine for several months but no blood in the urine and no dysuria. She has occasional knee pain since her knee replacement but does not take NSAIDs on a regular basis. No significant family history of kidney disease. She admits to being compliant on current medication regimen but has not had her blood pressure checked in several months.

Current Medication: Lasix 80 milligrams daily.; low dose aspirin daily; Prinivil 40 milligrams daily; simvastatin 40 milligrams q.h.s.; Tylenol p.r.n.

Past Medical History:
Hypertension since 1980s
Obesity
Dyslipidemia
S/P Right Knee Replacement 2003
New-onset proteinuria, as above

Social History:
Married, 4 children alive and well, smokes roughly 1 ppd since age 16, no alcohol intake, no illicit drug use.

Review of Systems: as per HPI

Laboratory Assessment:

Timed urine collection:	8:00 AM, 8/5/2010 to 8:00 AM, 8/6/2010 total urine volume 1780 mL/24 hours urine creatinine 60.7 mg/dL total urine protein 1.08 grams/Total volume Creatinine Clearance 125 ml/min.

Collected 9/4/2010

SODIUM LEVEL (SOD)	137		136-146	mMOL/L
POTASSIUM LEVEL (POT)	4.5		3.5-5.0	mMOL/L
CHLORIDE (CHLOR)	101		98-108	mMOL/L
CO2 (CO2)	29		22-34	mMOL/L
UREA NITROGEN (UN)	12		8-20	MG/DL
CREATININE LEVEL (CREAT)	0.6		0.5-1.0	MG/DL
GLUCOSE LEVEL (GLUC)	151	H	73-110	MG/DL
CALCIUM LEVEL (CAL)	9.2		8.6-10.3	MG/DL
PROTEIN LEVEL (PROT)	7.0		6.0-8.3	G/DL
ALBUMIN LEVEL (ALB)	4.3		3.5-4.9	G/DL
AST (AST)	28		8-30	IU/L
ALT (ALT)	39	H	7-35	IU/L
ALKALINE PHOSPHATASE (ALK)	76		30-130	IU/L
BILIRUBIN, TOTAL (TBIL)	0.7		0.2-1.2	MG/DL
MAGNESIUM LEVEL (MAG)	1.8		1.5-2.4	MG/DL
PHOSPHORUS LEVEL (PHOS)	4.0		2.7-4.6	MG/DL
AFRICAN AMERICAN EGFR (B-EGFR)	139		> 59	ML/MIN
NON-AFRICAN AMERICAN EGFR (NB-EGFR)	115		> 59	ML/MIN
MPV NORMAL RANGE: 7.8 to 10.6 fl.				
White Blood Cell Count (WBC)	7.7		4.0-10.0	K/MM3
Hemoglobin (HGB)	12.9		12.0-16.0	G/DL
Hematocrit (HCT)	37.4		35.0-48.0	%
Platelet Count (PLT)	272		150-450	K/MM3
Red Blood Cell Count (RBC)	4.13		3.90-5.30	M/MM3
Mean Corpuscular Volume (MCV)	90.6		80.0-100.0	fl
Mean Corpuscular Hgb (MCH)	31.3		25.0-35.0	pg
Mean Corpuscular Hgb Conc. (MCHC)	34.6		30.0-37.0	G/DL
Red Cell Distribution Width (RDW)	13.1		11.5-15.5	%
Mean Platelet Volume (MPV)	7.6			fl

Collected 9/11/2010

PROTEIN URINE RANDOM (PROTU2)	918.3			MG/DL
CREATININE URINE RANDOM (CREATU)	158.3			MG/DL
PROTEIN/CREAT URINE RATIO (PROCRE)	5.80	H		
Color (Urine) (UCOLOR)	Normal		Normal	
Appearance (Urine) (APPEAR)	Normal		Normal	
Specific Gravity (Urine) (SP GR)	1.020		< 1.035	
pH (Urine) (UPH)	6		4.6-8.0	
Leukocyte Esterase (Urine) (LEUK EST)	NEG		NEGATIVE	LEU/UL
Nitrite (Urine) (NITRITE)	NEG		NEGATIVE	
Protein (Urine) (PROTEIN)	500mg/dl	*	<30mg/dl	
GLUCOSE (Urine) (GLUCOSE)	NEGATIVE		NEGATIVE	
Ketones (Urine) (KETONES)	NEG		NEGATIVE	
Urobilin (Urine) (UROBILIN)	< 1mg/dl		<2 mg/dl	
Bilirubin (Urine) (BILIRUBIN)	NEG		NEGATIVE	
Blood (Urine) (BLOOD)	NEG		NEGATIVE	

She consents to NEPTUNE and has kidney biopsy.
One week later, pathology report is available (see separate text file).

15. Appendix B. Pathology Manual of Procedures

Scientific information compiled by Dr. L. Barisoni

Research Coordinator questions can be addressed by the NEPTUNE Program Manager at 1-877-9-NEPTUNE (734-615-5021)

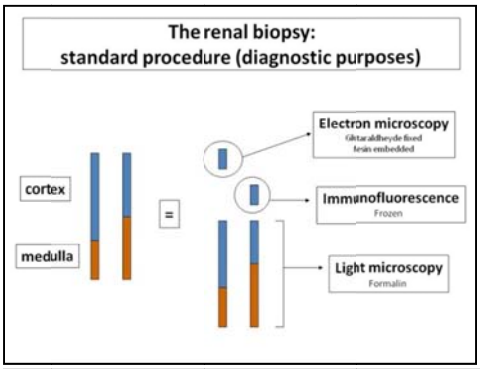
Renal biopsy procedure

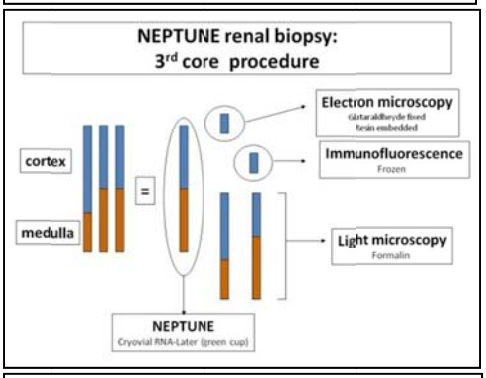
Goals:

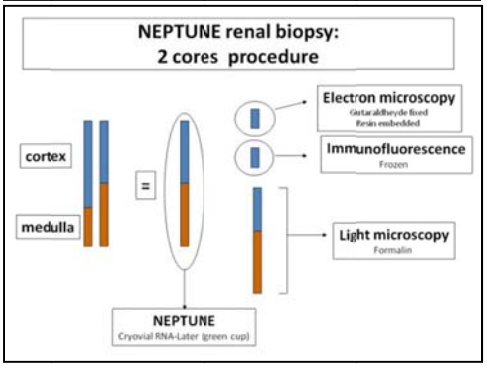
1. Obtain diagnostic material, including tissue for Light Microscopy (LM), Immunofluorescence (IF) & Electron Microscopy (EM).

2. Preserve integrity of diagnostic material to fulfill adequacy criteria for NEPTUNE pathology evaluation (LM, IF & EM).

3. Obtain research core without compromising diagnosis. Research core should immediately be placed in RNA later. Possibly within 30 seconds.







NOTICE OF RESEARCH PARTICIPATION
KIDNEY SPECIMENS

LOCAL FORM ONLY

INCLUDE WITH CLINICAL SPECIMENS FOR PATHOLOGY

Patient Name:_____ **Date:**_____
(Last) (First) (MI) (MM/DD/YYYY)

Patient ID:_____ **NEPTUNE Study ID:** ____ **- 26609 -** _____ **-** _____
(Indicate YOUR Medical Center's Medical Registration Identifier)

The above-named patient has consented to participation in NEPTUNE (**NEP**hrotic Syndrome S**tu**dy **Ne**twork). Participation in this study requires an additional renal core to be obtained during the clinically-indicated biopsy procedure. The additional core will remain with the research coordinator named below, at -80 C.

This additional core will not be released for research use prior to the renal pathologist's preparation, review, and histopathological diagnosis and if necessary, the core will be returned for diagnostic use (sample immersed in RNA-Later, valid for light microscopy only) by contacting the research coordinator named below. Please contact your site research coordinator (identified below) when you have completed your diagnosis and slides are available for pick-up.

Research Coordinator: *please print legibly*

First Name:		
Last Name:		
Work / cell phone:	Work:	Cell:
Pager: (if applicable)		
Email:		

Sample available for research: ☐ **Yes** ☐ **No**

Pathology release signature:	
Pathologist name printed:	
Treating Physician:	
Name printed:	

15.A. *Requested Pathology Materials*

In addition, NEPTUNE is requesting the following processed and unprocessed slides for research indications only:

	Glass Slides	EM Material	IF Material
To be returned within 2 weeks	• All LM glass slides available processed for LM • Thick sections of tissue processed for EM • H&E from frozen sections of tissue processed for IF		
	• Minimum of 4 unstained slides	CD with copy of digital EM images (preferred) *or* EM prints	CD with IF images if available and with pathology report

Fee to be paid to local/center pathology department for each case = $25

Compliance with HIPAA regulations:

Goal: Replace personal identifiers from all pathology material and use Neptune Study ID.

Strategy: All glass slides require NEPTUNE pre-printed labels to cover original label on the glass slide (please see instructions pps. 5-7).

All patient identifiers need to be deleted from each EM image or print before scanning or shipping and NEPTUNE Study ID placed on each print or image. All patient identifiers must be deleted from digital images before shipment (please see instructions pps 8-12).

Patient identifiers should be deleted from scanned pathology report and replaced with NEPTUNE Study ID (study ID is located on Form 11A-1 at (A) page 2).

Caution: cropping portions of digital images may be reversible, please ensure that the information is truly deleted.

In addition, NEPTUNE is requesting the following processed and unprocessed slides:

- Glass slides
  - All LM glass slides available processed for LM
  - Thick sections of tissue processed for EM
  - H&E from frozen sections of tissue processed for IF
  - Minimum of 4 unstained slides
- EM material
  - CD with copy of digital EM images (preferred) or CD with scanned EM images
  - or EM prints
- IF material
  - CD with IF images if available and with pathology report (can be same CD containing EM)
  - or copy of de-identified pathology report

Fee to be paid to local/center pathology department for each case = $25

Compliance with HIPAA regulations:

Goal: Replace personal identifiers from all pathology material and use Neptune Study ID.

Strategy: All glass slides require label to cover original label on the glass slide. New label from participant kit includes the following:

- Neptune Study ID
- Blank level indicator (to be completed on site)

All patient identifiers need to be deleted from all EM prints before scanning or shipping and NEPTUNE Study ID placed on each print or image. All patient identifiers must be deleted from digital images before shipment (please see (A) page 2).

Patient identifiers should be deleted from scanned pathology report and replaced with NEPTUNE Study ID (please see (A) page 2).

Caution: cropping portions of digital images may be reversible, please ensure that the information is truly deleted.

Note: Any biopsy with one or more slides, prints, reports, and images with personal identifiers will be returned to the originating site (including portions that have been de-identified) for corrections.

Shipment of pathology material to NIH – please send all materials in one shipment (items 1-3, Form [11B]). Please include the self-addressed Fed-ex label for the return shipment from the participant kit.

Mailing address for pathology materials:

Ms. Lisa Swearinger
Kidney Disease Section
10 Center Dr, Room 3N116 NIH
Bethesda, MD 20892-1268

Tel: 301-496-3092 lisas@intra.niddk.nih.gov

NIH protocol: scanning and storage of image files

When kidney biopsy material arrives at NIH, Ms. Swearinger will receive and record what is received in a dedicated logbook. **Any discrepancies between the package contents and the manifest will be reported by Lisa Swearinger to the site research coordinator within 24 hours.**

- LM: Kidney biopsy glass slides will be scanned on Aperio image system at 40X. Order will be according to level. Slide label should include Neptune Study ID and level. Files will be uploaded into the database.
- EM: Digital files will be uploaded directly. Electron microscopy prints will be scanned on flat bed scanner. Prints or digital files should include Neptune Study ID.
- IF: Images will be uploaded directly. Files should include antibody used and Neptune Study ID.
- Biopsy report including immunofluorescence description will be uploaded (scanned if necessary). Neptune Study ID should be included.
- NCI Slide Path database: Folders for each study site, and folders within for each Study ID.
- NCI server: uses RAID 5 back-up (redundant array of inexpensive disks) – 4 copies – as well as tape backup.
- **Kidney materials will be returned to the originating institution via UPS within 2 weeks of arrival**; if for some reason this cannot be achieved, an email will be sent to the originating PI with an explanation and anticipated send date.

- Images can be accessioned by the NIH approved staff and NEPTUNE Pathology Committee members. External access will be available via LDAP (Lightweight Directory Access Protocol - same pathway as eRA commons) – including password support. Each approved pathologist user will have a personal password.

RESEARCH COORDINATORS

SLIDE HANDLING & PREPARATION

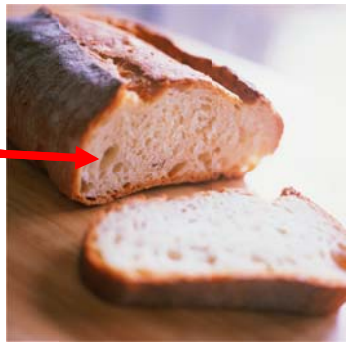
The NEPTUNE Site Research Coordinator should make arrangements with the local pathology team to be alerted when the NEPTUNE Study Participant's slide reading is complete. Local details may supercede the following description, please work with the NEPTUNE Clinical Program Manager and your site as necessary.

NOTE: Glass slides are fragile! Please take precaution when transporting and preparing for shipment.

The slides will likely be received on a tray. For the purposes of "re-labeling" there will be various slides; however, the information most necessary to transfer when each slide is de-identified is the NEPTUNE participant study ID, and the slide LEVEL (sequential series). Research Coordinators will need to be able to identify stained versus non-stained slides (BLANKS), as well as decipher the local pathology site's level-based ordering rubric.

If considering the slides as a loaf of bread,  each slice represents a slide "level". In an effort for the NEPTUNE Pathology Committee to re-construct 3-D images from the scanned slides, it is necessary to label each "slice" of bread sequentially to line up physiological cell markers and disease anomalies.

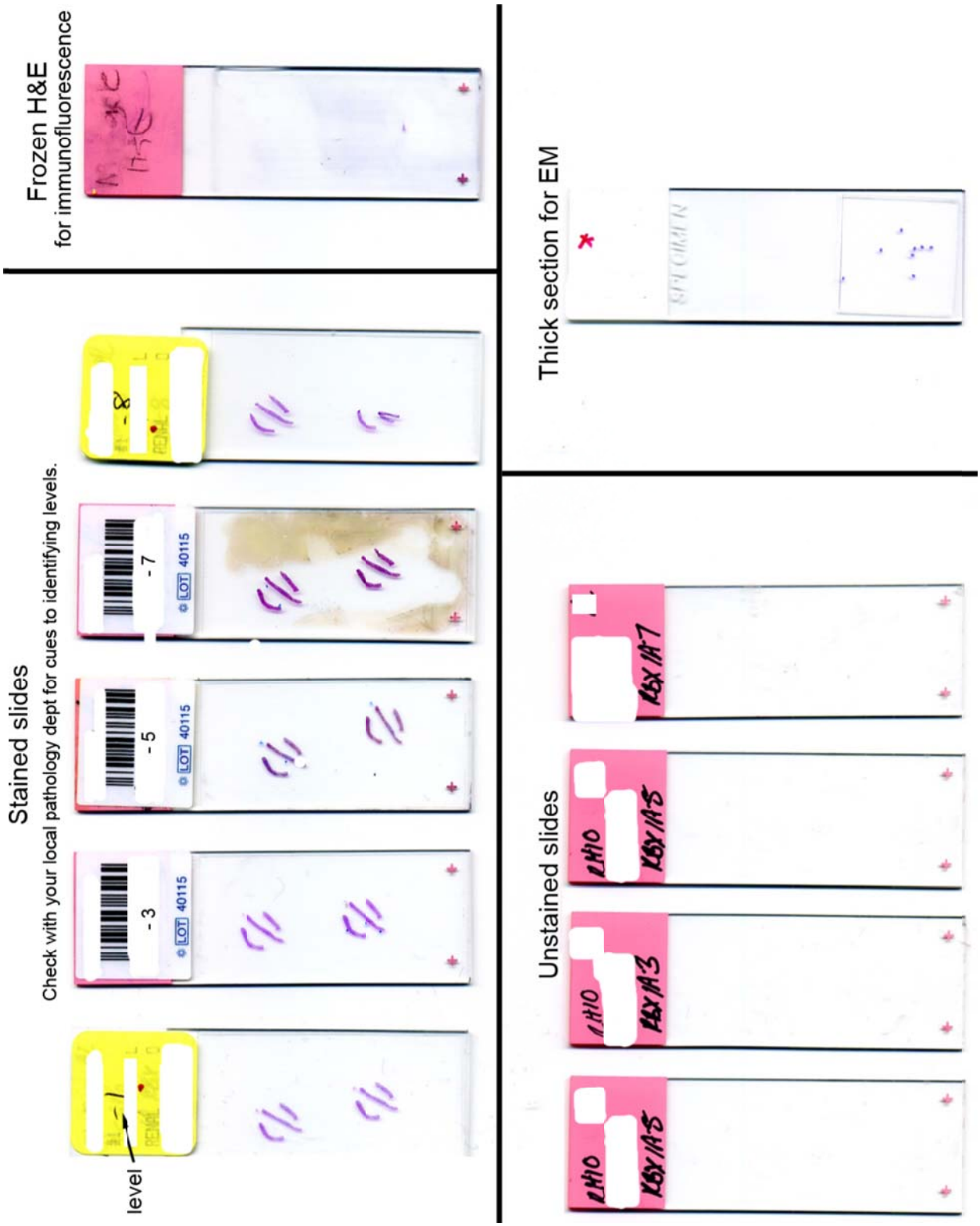
Analogy: an air bubble in the bread represents a glomerulus



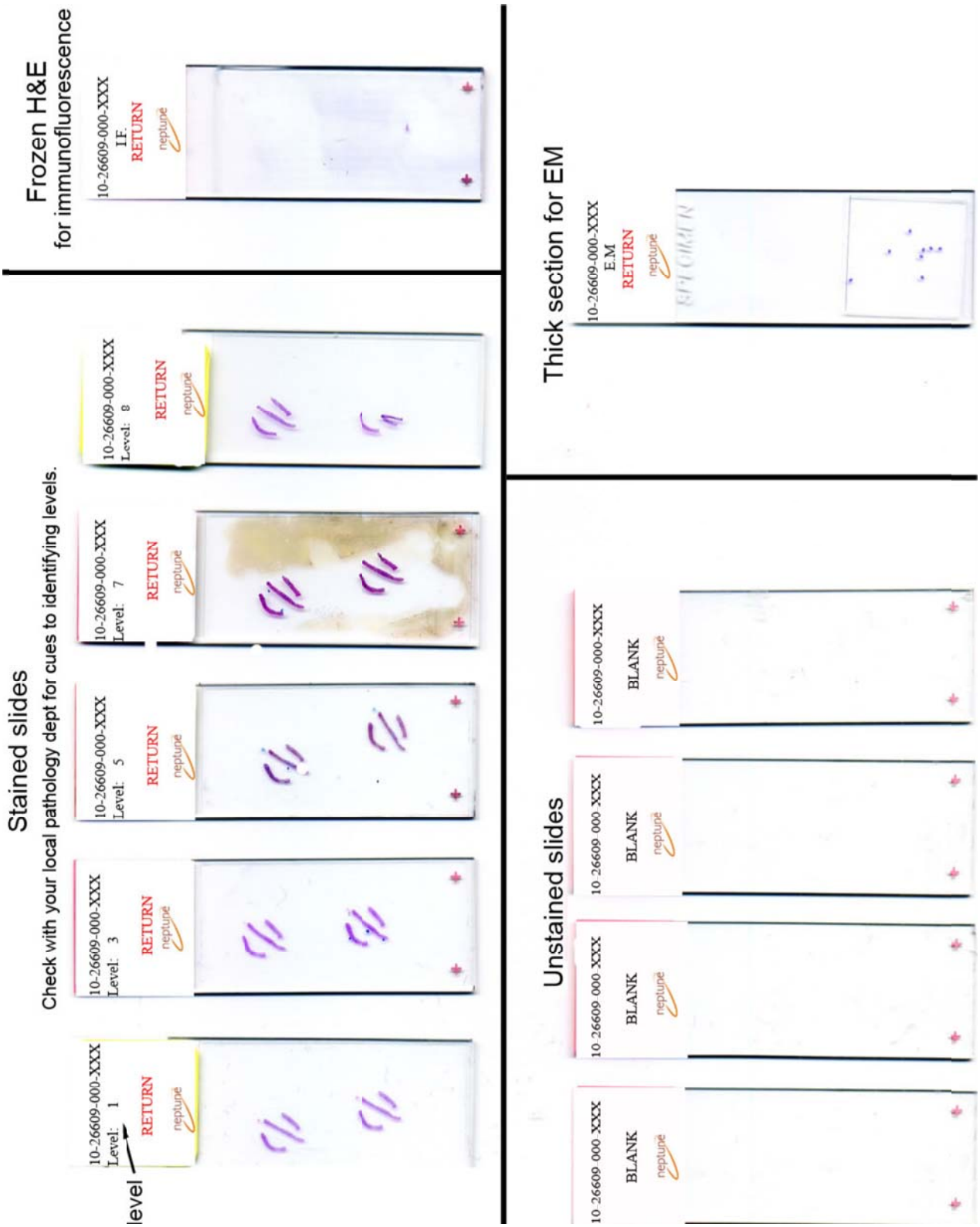
Place the study ID label *over* your local site's patient identifier taking note of the slide "level". If possible, it is recommended Research Coordinators meet initially with the site renal pathologist or a pathology technician to discuss identifying this essential detail. Please refer to slide set on the following page for reference.

In the stained slides area note the number details "1" - "8" indicating corresponding levels, respectively. When applying the NEPTUNE study participant label, be sure to write (with permanent pen, prior to transferring labels) the numbers identified for the NEPTUNE Participant's slides, in the respective blank Level: ____ area.

"Identified" slides to be re-labeled for NEPTUNE use.



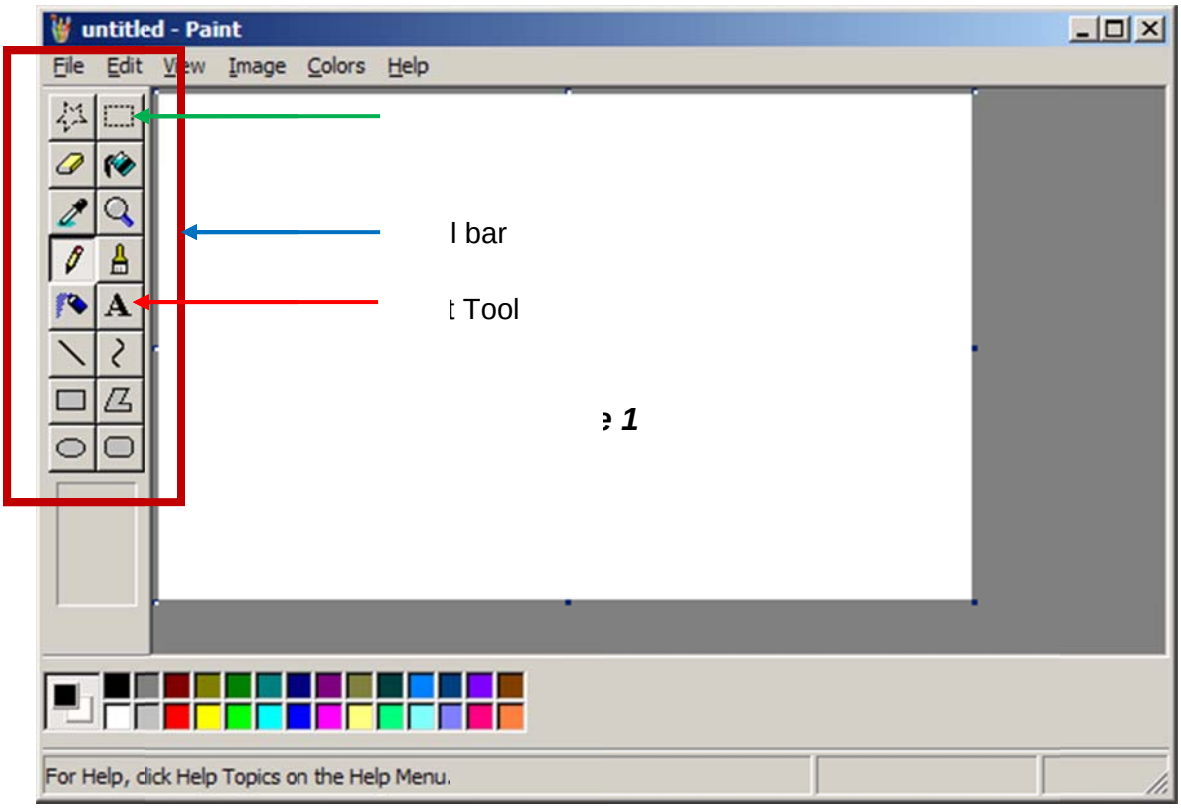
"De-identified" slides prepared for shipment to NIDDK Histopathological Archive for scanning and NEPTUNE study use.



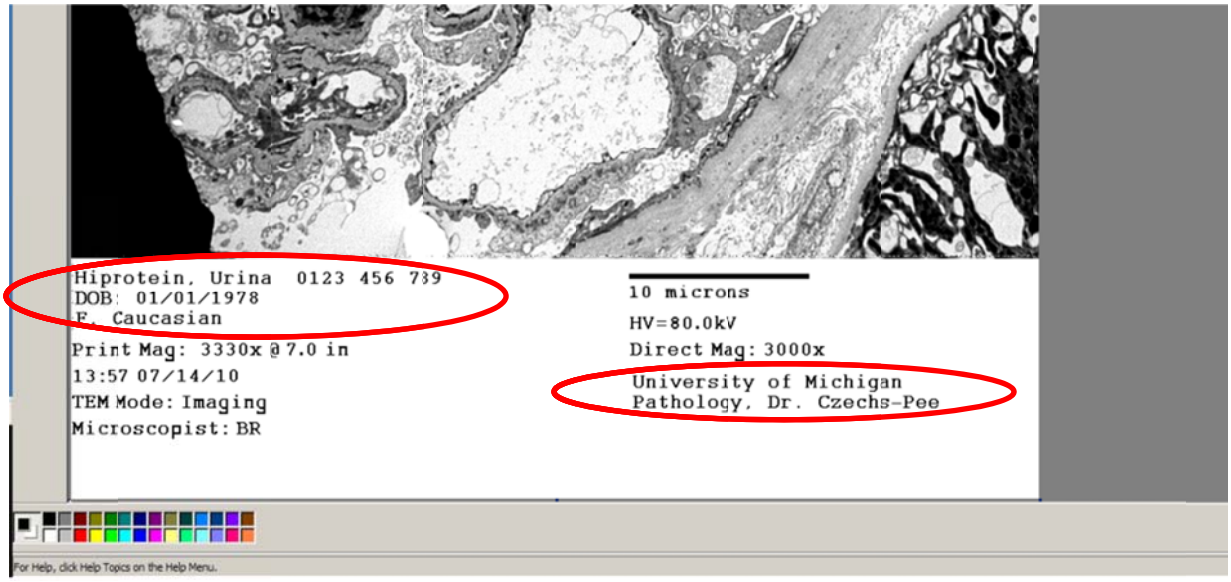
ELECTRON MICROSCOPY RE-LABELING INSTRUCTIONS

1. Digital Images

a. Open “PAINT” or a similar free image-adjusting software.



b. Open the EM document and review the information, noting any details which are “Identifying”:



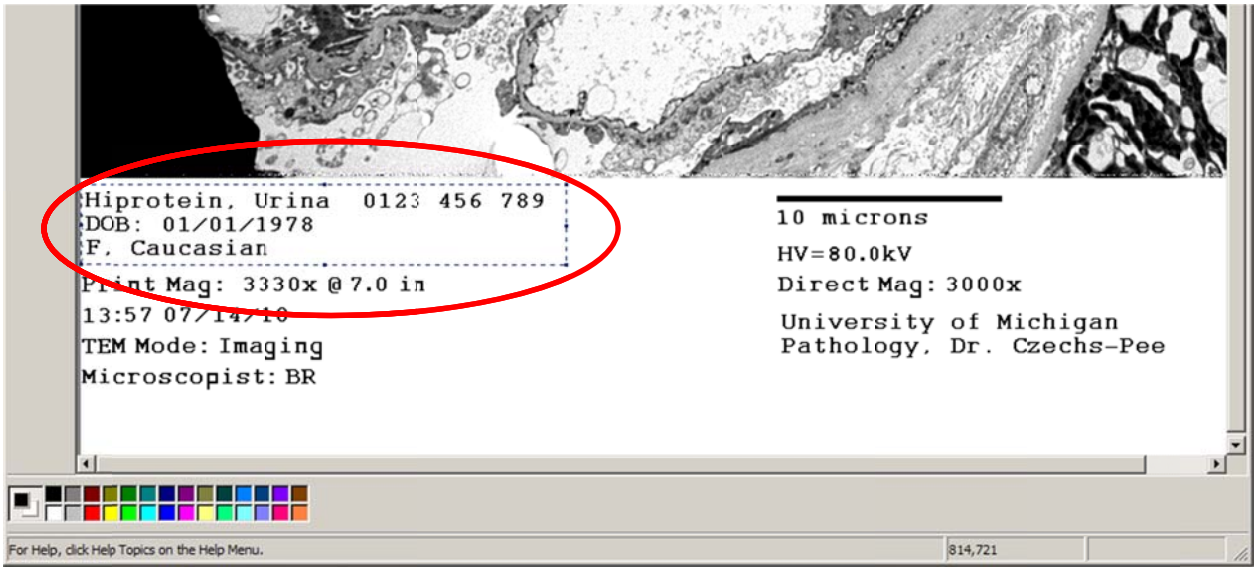
c. Review the image:

In the above image, Ms. Urina Hiprotein and her medical registration number 0123 456 789 must be removed. Other information which must be removed includes:

- Date of birth
- Gender identification (F)
- Racial identification (Caucasian)
- Site Identification by name (University of Michigan)
- Pathologist's name (Dr. Czechs-Pee)

d. Selecting/Deleting identifiable information: From the tool bar on the left of image 1 (this may vary at your site, depending on default settings), click on the "Select Tool". When over the image, the arrow becomes a cross-hair.

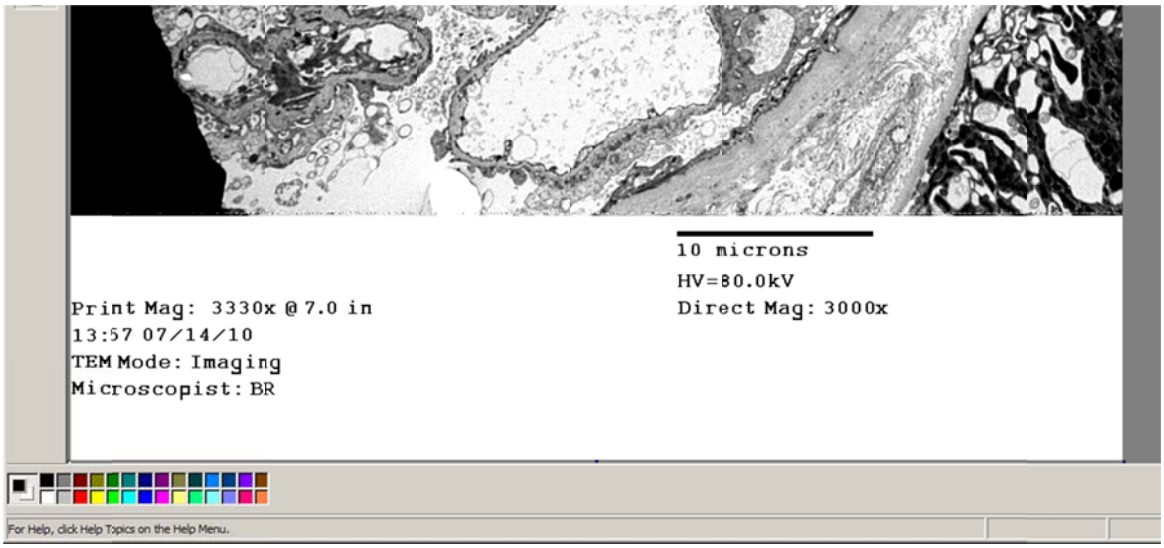
Move your mouse over the beginning of the text to be removed and click. Hold the click key on the mouse while dragging to select all text you would like to delete (see dashed box below).



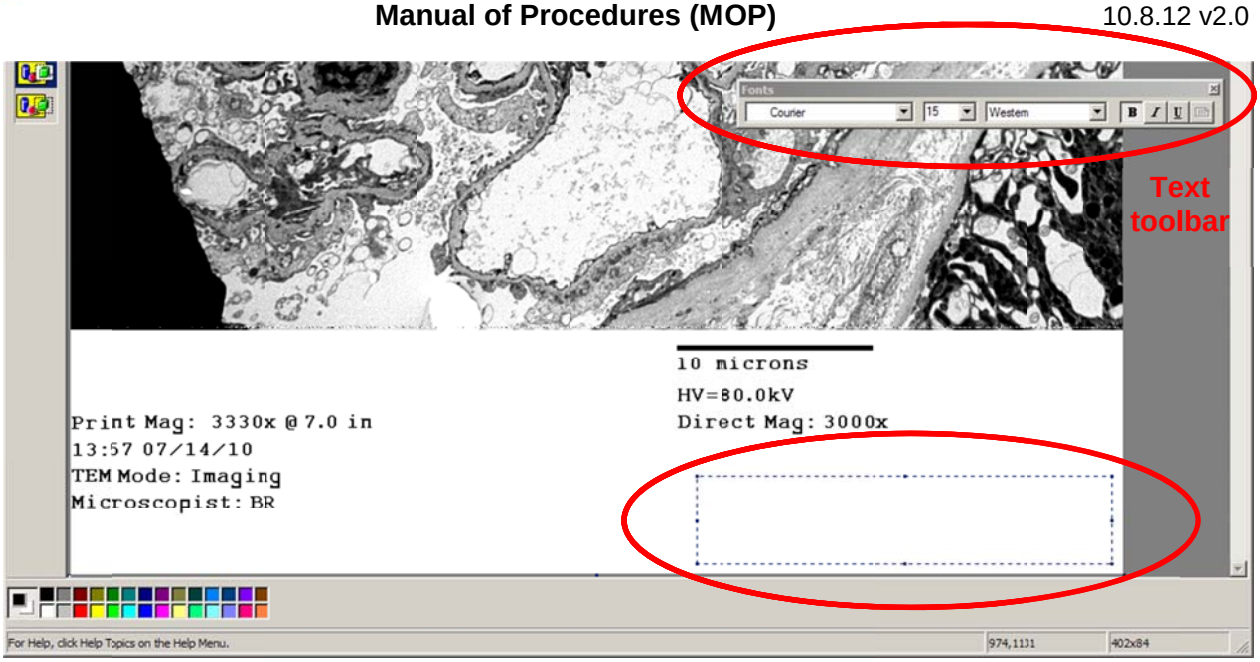
Release the mouse and the selected area will remain. The selection can be deleted by:

- Right clicking on the mouse and selecting “Cut”; or
- From the top menu bar, selecting “Edit” and choosing “Cut”; or
- Pressing “Ctrl-X” simultaneously

Repeat step d. above as necessary to remove all identifying information until the image resembles:



e. Re-labeling EM images with NEPTUNE Study ID: From image 1 above, locate the “Text Tool”. Click on the tool and then move the mouse to the LOWER RIGHT CORNER of the image. Drag a rectangle by clicking on the mouse and enlarging the box (see below):



Once the box is drawn, release the mouse key and type the following details:

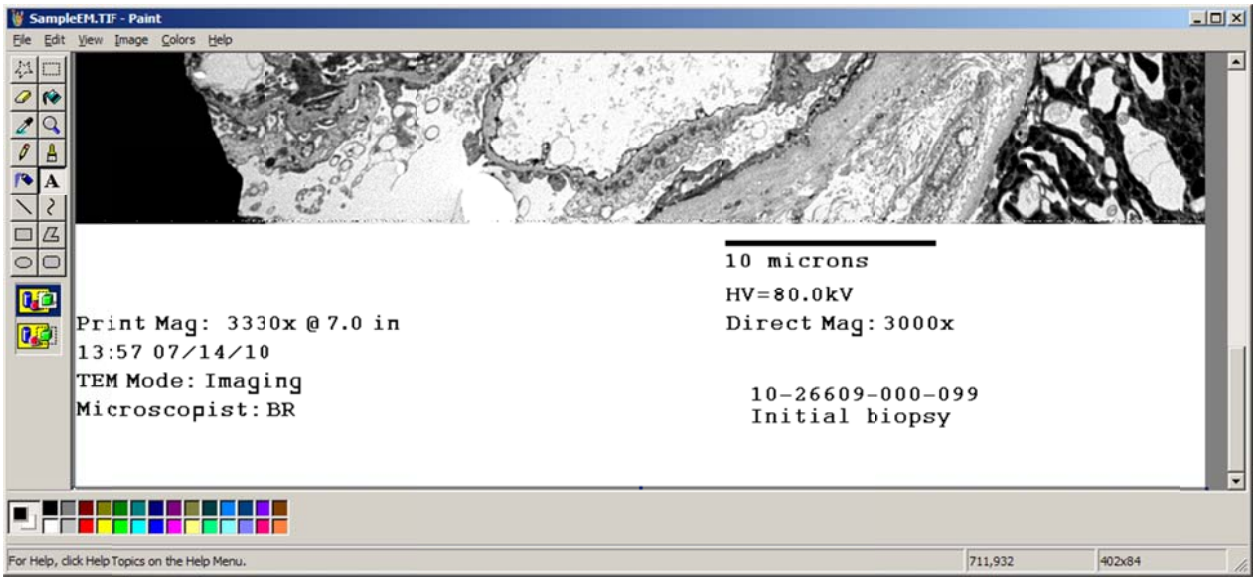
- Participant Study ID (10-26609-Site-StudyPt)
- Initial Biopsy *

***If this is a follow-up biopsy at a later time in the study (not the enrollment or initial biopsy visit), please indicate as "Post-time biopsy" with time in months, e.g., "Post 24-mos biopsy".**

If you are unable to see the Text toolbar above, you may need to click the "View" dropdown menu and select "Text Toolbar". Please use the following:

- Courier
- 15
- Western
- Bold

The final study image should resemble as follows:



f. Taking care to **not overwrite the original** image (do not just click “save”), please save the modified image by selecting:

File >
Save as>

The file name should be the Participant Study ID appended with the image number of the total quantity of images as follows:

- 10-26609-000-099_1of4
- 10-26609-000-099_2of4
- 10-26609-000-099_3of4
- 10-26609-000-099_4of4

2. **EM Prints**

a. Sites without digital images of the EM pathology:

1. Please obtain the prints from your site pathologist and enclose in the 9 x 12 inch envelope included in your kit (only sites with prints will have this envelope).
2. Place all images between the 2 cardboard pieces to protect the images from being bent in transit.

b. De-identification will take place at the NIDDK histopathology archive (a third party will be scanning and immediately de-identifying via the above-described method) and prints will be returned to your site.

PATHOLOGY REPORT DE-IDENTIFICATION INSTRUCTIONS

3. **Electronic Pathology Reports**

a. If your site has an electronic record of the kidney biopsy report:

1. Open the pathology report on your desk top;
2. Open a blank Microsoft office document, or similar text editing software;
3. In the pathology report, select ALL text, copy (usually <CTRL+C> on most PC systems) and return your cursor to the text editing software
4. Paste all <CTRL+V>
5. Remove all identifying information from the report, including:

- Patient hospital identifier
- Reference to age, gender (excluding “pediatric” or “adult”)
- Race
- Ordering physician’s name/initials
- Pathologist name/initials
- Other information deemed identifiable
- Any details identifying site (name(s) of hospital(s), addresses of healthcare institutions, phone numbers, non-treating physicians names, etc)

Information can be de-identified by completing deleting the text (Please insert <DELETED TEXT> when you do this, so it is clearly understood details are missing).

b. If your site has a printed record of the kidney biopsy report:

1. Obtain a legible copy of the report;
2. Copy and complete original for the participant’s study chart (or shadow chart);
3. You should have 2 copies: one for the NIDDK, one for the study chart
4. On the NIDDK copy, using a black permanent marker, draw a line through all identifying details (listed above). Please be sure this de-identifying includes removing details from institutional letterhead if applicable).

Once all images and the local pathology report has been de-identified, please burn these documents and the de-identified pathology report to the enclosed, pre-labeled NEPTUNE CD. This should be sent to the NIDDK with the pathology slides in the pre-addressed. The pathology report can be copied and pasted from an electronic file into a word file, please see appendix C to review an example of details removed from the report.

De-identified Pathology Report Example

HISTORY:

The patient is a [redacted] year-old <DELETED TEXT> with a several year history of proteinuria and nondysmorphic hematuria. [redacted] [redacted] sister has similar signs and symptoms.
Urinary protein:creatinine ratio has ranged from 5 to 6, serum albumin has been 2.5 to 3.5 gm/dL, serum creatinine to 0.7 mg/dL. [redacted] has edema. ANA is positive, otherwise all serologies negative.

GROSS:
------
1. Labeled with patient's name and hospital registration number. Received in formalin are three tan cores ranging from 0.5 cm to 1.0 cm. (3ns)
2. Labeled with patient's name and hospital registration number. Received in Michel's fixative are four, 0.1 cm, tan-gray, soft tissue bits submitted for immunofluorescence. (4ns)
3. Labeled with patient's name and hospital registration number. Received in glutaraldehyde are four tan cores 0.1 cm each; held for processing in the EM lab. (4ns)[redacted]

[redacted] mm/dd/yyyy

MICROSCOPIC:
LIGHT MICROSCOPY:

Sections are stained with H&E, PAS, trichrome and Jones-Silver. There are three cores of renal cortex that contain thirty glomeruli, eight of which are globally sclerotic. An additional six glomeruli display focal segmental sclerosis with obliteration of capillary lumina, excess matrix and adhesion to Bowman's capsule. The remaining glomeruli appear mildly enlarged with patent capillary lumina and glomerular basement membranes of normal thickness and contour. Tubular atrophy and interstitial fibrosis involves approximately 10% of the renal cortex. Collections of foam cells can be seen in the interstitium in a multifocal pattern throughout the tissue. Mild tubular injury can be identified in patchy locations. A few small arteries are sampled and appear normal.

IMMUNOFLUORESCENCE MICROSCOPY:

Direct immunofluorescence examination of the renal biopsy specimen (two glomeruli) with FITC-conjugated antisera for IgG, IgA, IgM, C3, C4, C1q,albumin and fibrinogen revealed: Controls for IgG, IgA, IgM, and C3 are positive.

IgG: Negative.
IgA: Negative.
IgM: Negative.
C3: Focal glomerular positivity (nonspecific).
C1q: Negative.
C4: Negative.
Albumin: Negative.
Fibrinogen: Negative.
Kappa: Negative.

Lambda: Negative.

ELECTRON MICROSCOPY:

All of the tissue submitted for electron microscopy was embedded and examined at the thick section level. One available glomerulus is selected for ultrastructural evaluation.

The ultrastructural preservation of the tissue is adequate. Glomerular capillary lumina are patent and mesangial areas are normal in size and cellularity. The glomerular basement membranes are diffusely thickened with an average thickness of 116 nm (range 79 to 142 nm). A few portions of the basement membrane display mild textural irregularities including internal lucent rarefactions and slight lamellation. Some portions of the basement membrane are focally thickened and wrinkled. Podocyte foot process effacement involves approximately 70% of the glomerular capillary surface. Podocytes appear hypertrophic and reactive with lipid and protein resorption droplets and focal microvillous transformation.

MICROSCOPIC DIAGNOSIS:

Renal biopsy, light, fluorescence and electron microscopy:

1. Focal segmental and global sclerosing glomerulopathy, moderate, with diffuse thinning and segmental lamellation and thickening, consistent with hereditary nephritis.
2. Tubular atrophy and interstitial fibrosis, mild.

COMMENT:

The immunofluorescence findings provide evidence against glomerular disease of the immune complex type. Electron microscopy reveals predominant thinning and focal thickening of the basement membranes with some irregularities. This, in conjunction with the light microscopic findings of focal and global glomerular sclerosis and multifocal collections of interstitial foam cells, and a XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX hereditary nephritis often have a predominantly thin basement membrane phenotype, as appears in this case.

[redacted]

I, [redacted] the signing staff pathologist, have personally examined and interpreted the slides from this case.

16. Appendix C. Neptune Study Worksheet References

16.A. General Information

Worksheets have been created for each study visit, in parallel with Velos Case Report Forms (CRFs), to serve as source documents for study data.

16.A.1. Using Worksheets

All worksheets for a particular visit should be printed off by the RC prior to the scheduled visit and carried to the visit as most information will be completed in the presence of the participant. The remaining information may be pulled from the participant's medical record. Sites electing to do local data entry should transfer all worksheet information to the corresponding Velos CRF within one week. Sites approved for central data entry should securely transmit completed worksheets to the NEPTUNE DACC within one week of study visit, with the exception of any lab worksheets, which have a +/- 30 days study visit window.

Forms 2B, 3, and 5 should be updated at every visit.

Every field in the worksheets should be completed. If the answer to a question is unknown or not applicable, please either check the Unknown/Not Applicable box or enter UNK or NA into the space provided.

Detailed instructions on how to complete each question on each worksheet are outlined below. Please complete all worksheets with a black or blue pen (No pencil!)

Corrections to data entered into worksheets should consist of a SINGLE line drawn through the incorrect data, dated and initialed by the NEPTUNE study team member, with the correct data written neatly nearby.

Example:

Incorrect	Incorrect	Correct
~~45 mg PO~~	~~45 mg PO~~	~~45 mg PO~~ 2/23/12 CCL 25 mg PO

16.B. Worksheet List/ Completion by Visit

The following is a complete list of worksheets/forms that will be used to gather information about NEPTUNE Study Participants. Some worksheets/forms will be used at several visits and some will only be used as needed. Original, completed worksheets should be maintained in the participant's study chart as source documents.

- **Recruitment/Pre-Screening Visit [V0]**
  - Form 1 Eligibility Assessment Worksheet (Part I)
  - Form 1 Eligibility Assessment Worksheet (Part II), pre-consent
- **Screening/Eligibility Visit [V1]**

- Form 1 Eligibility Assessment Worksheet (Part II), post-consent
- Form 2A Velos Registration Worksheet
- Form 2B Contact Information Worksheet
- Form 5 Concomitant Medications Log

- **Baseline Visit [V2]**
  - Form 2B Contact Information Worksheet (updated at every visit)
  - Form 3 Healthcare Provider Information Worksheet
  - Form 4A Baseline Participant Information
  - Form 4B Baseline Family History
  - Form 4C Baseline Clinical Information
  - Form 5 Concomitant Medications Log Worksheet (updated at every visit)
  - Form 6A-E Quality of Life Worksheet
  - Form 7 PROMIS Assessment Worksheet
  - Form 8 Baseline Biospecimens Worksheet
  - Form 10 Baseline Labs Worksheet
- **Biopsy Visit [V3]**
  - FORM 11 KIDNEY BIOPSY SPECIMENS
  - Form 11A Kidney Specimens Worksheet
  - Form 11B Outgoing Slides Shipment Form
  - Form 11C Incoming Slides Shipment Form
  - V3 Biopsy Specimens Form
- **Follow Up Visits [V4-13]**
  - Form 2 Contact Information Worksheet (update)
  - Form 3 Healthcare Provider Information Worksheet (updated at every visit)
  - Form 5 Concomitant Medications Log Worksheet (update
  - Form 13A Follow Up Participant Information
  - Form 13B Follow Up Family History
  - Form 13C Follow Up Clinical Information
  - Form 14 Follow Up Biospecimens Worksheet
  - Form 15 Follow Up Labs Worksheet
- **Additional Worksheets/Forms (Used as Needed)**
  - Form 9 Adverse Event Worksheet (This should be used to record all Adverse Events, both serious and non-serious)
  - Local Institutional Authorization to Release Patient Information (This should be used if the patient requests medical records from the NEPTUNE institution either for themselves or for another institution)
  - Local Institutional Authorization to Request Information (This should be used to retrieve information on the patient if the patient is hospitalized or seen by another clinic/institution while on the NEPTUNE Study)

16.C. Worksheet References

Please refer to the following pages for detailed instructions for the completion of each worksheet. Worksheet data should be transferred into Velos within 7 days of the study visit for sites completing local data entry. Sites approved for Central Data Entry (CDE) should refer to the CDE Appendix for specific instructions for transferring select data to the NEPTUNE DACC.

16.C.1. Form 1 Eligibility Assessment Worksheet (Part I [V0])

***Please see the reference below for a complete description of each numbered question.**

1 Patient Initials: _____ 2 Site ID: _____

3 Pre-Screening Date [V0]: _____ *(Part I)* 4 Date of Screening Contact [V0]: _____ *(Part II)*

ELIGIBILITY ASSESSMENT

To Be Completed During Pre-Screening (For Office Use Only)

PRELIMINARY DEMOGRAPHIC INFORMATION 5				Male		Female
Age:	6	Years	If < 24 months:	7		Months

8 **Ethnic background:** (*Check only one*)		Hispanic or Latino (**See Below*)
		Not Hispanic or Latino

9 **Racial background:** (*Check all that apply*)				
	American Indian/Alaskan Native		Asian/Asian American (**See Below*)
	Black/African American (**See Below*)		Native Hawaiian/Other Pacific Islander
	White/Caucasian		Don't Know

INCLUSION CRITERIA *(All questions must be answered yes for the individual to be eligible)*

Yes	No						
10		Is patient scheduled for a renal biopsy?					
11		What is the indication for biopsy? *(please check one)*					
			Proteinuria		Steroid resistant NS		Steroid dependent NS
			Frequently Relapsing NS		Proteinuria w/decreased GFR		Other: _____
12		Does patient have documented urinary protein excretion ≥ 500 mg/24 hours or spot protein:creatinine ratio ≥ 0.5 mg/mg at the time of diagnosis or within 3 months of the screening visit?					

13 **24 Hr Urinary Protein Excretion**				*OR* 14 **Spot Protein/Creatinine Ratio**	
Protein		Units:		Urine Protein to Creatinine	
Creatinine *(enter NA if Creatinine not available)*		Units:		Date Measured	
Date measured:					

EXCLUSION CRITERIA *(All questions must be answered no for the individual to be eligible)*

Yes	No	
15		Has patient had a prior solid organ transplant?
16		Does patient have clinical, serological or histological evidence of systemic lupus erythematosus (SLE) as defined by the ARA criteria?
17		Does patient have clinical or histological evidence of: • Alport • Nail Patella • Diabetic Nephropathy • IgA-nephritis • Monoclonal gammopathy (multiple myeloma) • Genito-urinary malformations with vesico-uretheral reflux • Renal dysplasia
18		Does patient have known systemic disease with life expectancy less than 6 months?
19		Does patient currently live in a prison, nursing home, skilled nursing facility, or other institutional setting?

Form 1 Eligibility Assessment Worksheet v3.1 Feb-2012 Page 1 of 3

16.C.1.a. *Suggested Screening Language*

When locally approved by a site's IRB, the following is a brief overview of the NEPTUNE study. This language can be used to assess a potential participant's interest in learning more about the study without informed consent.

Suggested Screening Language

*** RC should have screened for items on PAGE 1 of Eligibility WORKSHEET in advance of eligibility questions for potential participant ***

Suggested Screening Language:

This is a study for Nephrotic Syndrome which includes FSGS, MCD, and MN. You qualify as a potential participant because you are *already* getting a renal biopsy. We would ask for your permission to obtain some additional renal tissue from that procedure, in addition to some blood and urine. We would like to collect blood and urine over the course of the study.

This study may require additional time or visits to [Healthcare facility]. Initially, there will be 13 total visits (year 1, every 4 months, years 2-5 every 6 months).

We would also ask for you to complete some questionnaires during some of the study visits and provide nail clippings.

Would you be interested to see if you are eligible to participate?

Would you be willing to sign an informed consent agreeing to be in the study after learning more about the study details?

16.C.2. Form 1 Eligibility Assessment Worksheet (Part II [V0])

1 Patient Initials: _____ 2 Site ID: _____

3 Pre-Screening Date [V0]: _____ (Part I) 4 Date of Screening Contact [V0]: _____ (Part II)

To be Completed With Patient the Day of Eligibility Assessment

How did the patient become aware of the study (please check one)? 20	☐	In Person	☐	Telephone
	☐	Website	☐	NephCure
	☐	Other:		

FINAL INCLUSION CRITERIA *(Questions must be answered yes for the individual to be eligible)*

	Yes	No	
21	☐	☐	Is patient willing and able to give a comprehensive informed consent after learning more about the study details?
22	☐	☐	If patient decides to take part in the study, are they willing to comply with study procedures and visit schedule?

Research Coordinator's assessment of patient's enthusiasm (please check one): 23	☐	High	☐	Medium
	☐	Low	☐	None
	☐	Unable to Determine		
If patient is interested in joining the study, do they have time today to review the consent? 24	☐	Yes*	☐	No* *(see below)*
	25 If no, Date:			
	Time:			

***If the patient signs informed consent , please request the following details for demographic reporting upon study enrollment:**

Ethnic background: 26 **(*Check only one*)**	☐	Hispanic or Latino *(*See Below)*		
	☐	Not Hispanic or Latino	☐	Not Reported
**If Hispanic or Latino (Check all that apply):* 27	☐	Mexican American or Mexican	☐	Dominican
	☐	Central American	☐	Spaniard or Portuguese
	☐	South American	☐	Other (specify)
	☐	Puerto Rican		
	☐	Cuban	☐	Don't Know

Racial background: **(*Check all that apply*)** 28	☐	American Indian/Alaskan Native	☐	Asian/Asian American (*See Below)
	☐	Black/African American (*See Below)	☐	Native Hawaiian/Other Pacific Islander
	☐	White/Caucasian	☐	Not Reported

This data must be entered into Velos CRF Form 4A

***If patient is not interested in participating, please remember to ask them to provide a reason for not participating (if they feel comfortable doing so). Please record this reason on the Screening Log.**

29 Coordinator Signature: _____ Date: _____

30 Coordinator Name & Title (Print): _____

Form 1 Eligibility Assessment Worksheet v3.1 Feb-2012 Page 2 of 3

16.C.3. Form 1 Eligibility Assessment Worksheet (Part III [V0/1])

1 Patient Initials: _____ 2 Site ID: _____

3 Pre-Screening Date [V0]: _____ (Part I) 4 Date of Screening Contact [V0]: _____ (Part II)

Research Coordinator Use Only:

Non-consenting patients	Yes	No	
Provided NephCure Brochure			31
Provided NEPTUNE Registry Brochure			32

	Consenting Participants					
	Consent for DNA:					
Obtain DNA from blood, urine and biopsy samples			33			
Create a cell line from blood cells			34			
Check DNA for genes related to kidney disease			35			
	Consent for:					
Maintaining Screen Failure Samples			36			
Release contact information to NephCure			37	If yes, date information sent:		
Share samples with NIDDK Biorepository			38			
	Information:					
Provided NephCure Brochure			39			
Provided NEPTUNE Registry Brochure			34			

Form 1 Eligibility Assessment Worksheet v3.1 Feb-2012 Page 3 of 3

16.C.3.a. *Form 1 Eligibility Assessment Worksheet Reference – Part I [V0]*

Part I of Form 1 should be completed as part of the initial screening process. All patients assessed or referred for the study should have a completed Form 1 Part I documented and transferred to the study screening log.

Header

1 Please enter the patient's initials.

2 Please enter the three digit site ID.

3 Please enter the date that eligibility pre-screening began (Part I).

4 Please enter the date of screening contact [V0] (Part II).

Preliminary Demographic Information

5 Refer to the individual's medical chart/records and check the appropriate box.

6 Refer to the individual's medical chart/records and enter in the correct age of the individual. If the individual is two years old or greater please enter the age in years.

7 If the individual is less than 24 months, please enter age in months.

8 Referring to the individual's medical chart/records check the appropriate box.

9 Referring to the individual's medical chart/records check the appropriate box.

Inclusion Criteria

10 Please check box "Yes" or "No" if a patient is *currently* scheduled for a renal biopsy.

11 Please review the patient's medical chart/records to determine the preliminary cause for the biopsy and mark one box.

12 Please check box "Yes" or "No."

13 If 24 hour urine results are being used verify inclusion, please record the most recent protein and creatinine results and units here. Additionally please record the date of the 24 hour urine collection.

14 If spot urine results are being used to verify inclusion please record the protein/creatinine ratio results here. Protein/creatinine ratio has no units. Additionally record the date of the spot urine.

Exclusion Criteria

15 Please check box "Yes" or "No" if patient has previously received a solid organ transplant (not including corneal transplant)

16 Please check box "Yes" or "No" for evidence available prior to the kidney biopsy.

17 Please check box "Yes" if participant has any of the listed diseases. Otherwise please check "No."

Alport Syndrome:	a genetic disorder characterized by glomerulonephritis, endstage renal disease, and hearing loss.
Nail Patella:	A genetic disorder characterized by small poorly developed nails and kneecaps. Persons with this syndrome may also develop kidney disease. Also referred to as Iliac Horn Syndrome, Hereditary Onychoostedysplasia, Fong Disease, or Turner-Kiser Syndrome.
Diabetic Nephropathy:	Kidney disease/damage resulting from diabetes complications.
IgA Nephritis:	A form of glomerulonephritis. Also known as Berger's Disease.

Monoclonal Gammopathy:	Condition where an abnormal protein is found in the blood and may progress over decades to other disorders. Also known as MGUS.
Genito-Urinary Malformation with Renal Dysplasia:	with Vesico-Ureteral Reflux: Some kind of malformation of the genitourinary tract with the addition of abnormal urine flow from the bladder to the ureters. Abnormal cellular differentiation of the renal tissue.

18 Please check box "Yes" or "No" if the medical record indicates a life expectancy of less than 6 months.

19 Please check box "Yes or No".

16.C.3.b. *Form 1 Eligibility Assessment Worksheet Reference – Part II [V0]*

When locally approved by a site's IRB, the NEPTUNE screening language provides an opportunity to provide patients and potential participant's a brief overview of the NEPTUNE study. This language can be used to assess a potential participant's interest in learning more about the study without informed consent.

20 Consult the participant and check the appropriate box.

Final Inclusion Criteria

To be assessed after the screening language is communicated to the patient.

21 Consult with the participant and check box "Yes" or "No" accordingly.

22 Consult with the participant and check box "Yes" or "No" accordingly.

23 After meeting with the potential participant, please select the appropriate box. Use the following criteria to differentiate between high, medium, low or none:

High:	Patient is very interested in the study and/or eager to participate.
Medium:	Patient seems genuinely interested in participating and is open to hear more about the study
Low:	Patient seems disinterested in participating and may or may not want to hear more about the study.
None:	Patient is indifferent about the study.
Unable to Determine	Patient does not provide any indication of interest/disinterest.

24 If the patient is interested to participate, ask him/her if they have time to review the consent and study details at this visit.

25 If they are interested but don't have time, please set up a time to review these items.

*** If the patient consents to the study, please request self-identified demographics to be entered into Velos upon registration:**

26 Ask the participant his/her self-identifying ethnicity and check the appropriate box.

27 If the participant has indicated Latino, please sub-classify as indicated, and check the appropriate box.

28 Ask the participant his/her self-identifying race and check the appropriate box.

29-30:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.3.c. *Form 1 Eligibility Assessment Worksheet Reference – Part III*

For all patients approached for the NEPTUNE study, consenting and non-consenting, both the NephCure brochure and the NEPTUNE registry brochure are to be provided. Please document that this has been done.

For consenting individuals, it will be important to document a participant's wishes regarding participation for DNA studies, creating cell lines, maintaining screen failure samples, releasing contact information to NephCure, and sharing samples with the NIDDK Biorepository.

Participants enrolled under Protocol Version 2.5 will need to be re-consented. This will need to be documented in the "Signed Informed Consent" link in Velos (see Velos manual of procedures in Appendix A). The new informed consent link will contain the fields for Form 1, Part III for documentation purposes.

Participants newly enrolled under Protocol Version 3.0 will not need to be re-consented; however, the documentation of the above items will still need to confirmed in the "Signed Informed Consent" link in Velos.

Research Coordinator Use Only

To be completed at the conclusion of [V0] (non-consenters):

31 Please record that the individual was provided The NephCure Brochure.

32 Please record that the individual was provided the NEPTUNE Registry brochure.

23 After meeting with the potential participant, please select the appropriate box. Use the following criteria to differentiate between high, medium, low or none:

To be completed at the conclusion of [V1] (participants who have signed consent):

33 Please record if the participant has consented to obtaining DNA and checking it for genes related to kidney disease.

34 Please record if the participant has consented to creating a cell line from their blood cells.

35 Please record if the participant has consented to maintain samples in the NEPTUNE study if they are determined to be "screen failure".

36 Please record if the participant has consented to releasing their contact information to The NephCure Foundation, and if yes, document the date information was emailed to: patientadvocate@nephcure.org

37 Please record if the participant has consented to send samples to the NIDDK Biorepository.

38 Please record that the individual was provided The NephCure Brochure.

39 Please record that the individual was provided the NEPTUNE Registry brochure.

16.C.4. Form 2A Velos Enrollment Worksheet

This form was created to assist sites in correctly registering participants into the NEPTUNE study Velos eResearch data management system.

***Please see the reference below for a complete description of each numbered question.**

Participant Initials: __1___ Visit Date (V1): ____2_____

Patient ID: _____3_____

VELOS ENROLLMENT

Patient ID: 4
(e.g. 008002)

Registration Details

First Name: 5
(UM only; DO NOT enter at outside sites)

Organization: 9
(verify your site appears here)

Last Name: 6
(UM only; DO NOT enter at outside sites)

Survival Status: 10 **Alive with Disease**
(always select Alive)

Date of Birth: 7
(MM/DD/YYYY)

Patient Facility ID: 11
(Outside sites only; patient's medical record number)

Gender: 8 ❒ Female ❒ Male

Study: 12 **10-26609**
(always select 10-26609)

Patient Study Status

Status: 13 **Enrolled**
(always select Enrolled)

Status Date: 14
(Date Informed Consent signed)

Patient Study ID: 15
(e.g., 11-26609-008-001)

Demographics

16 Marital status ❒ Single ❒ Married ❒ Divorced ❒ Widowed

17 Blood Type ❒ A ❒ AB ❒ B ❒ O
(if unknown enter UNK))

Assign your patient to the Protocol Calendar (click the "Edit Calendar/Date" link)

Treatment Details

18 Protocol Calendar: **NEPTUNE Calendar**
(always select NEPTUNE Calendar)

19 Patient Start Date:
(date of Baseline Visit, if known; otherwise, date of Biopsy)

20 Coordinator Name (Print): _____ Date: _____

21 Coordinator Signature: _____

Form 2A Velos Enrollment Worksheet V3 Feb-2012 Page 1 of 1

16.C.4.a. *Velos Enrollment Worksheet Reference*

Header

1 Please enter the participant's initials.

2 Please enter the date of the study visit.

3 Please enter the Velos ID (e.g. 004021)

Participant Details

4 Please enter the Velos ID (same as above)

5 Sites external to the lead site do not complete this field in Velos

6 Sites external to the lead site do not complete this field in Velos

7 Please enter the participant's date of birth in the format MM/DD/YYYY or use the calendar function.

8 Please indicate the participant's gender.

Registration Detail

9 Please verify your site auto-populates in the organization field of Velos.

10 Please always select "Alive with Disease" for Survival status when registering a new participant into Velos.

11 Please write and enter the participant's local medical record number in the Patient Facility ID field. This will allow the research coordinator to locate their participants in Velos should they need to do so without the Velos study ID..

12 Please always select 10-26609.

Patient Study Status

13 Please always select "Enrolled" when registering a new participant into Velos.

14 Please enter the date informed consent was signed in the Status Date field in Velos.

15 Please enter the NEPTUNE assigned participant study ID.

Demographics

16 If the participant indicates their marital status, please enter it here and in the respective field in Velos.

17 If the participant knows his/her blood type, please enter it here and in the respective field in Velos.

18 Please assign your participant to the NEPTUNE Calendar in the appropriate section in Velos.

19 If the date of the Baseline Visit [V2] is known, please enter as the Patient Start Date in Velos; otherwise enter the date of the biopsy.

20-21:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.5. Form 2B Contact Information Worksheet

***Please see the reference below for a complete description of each numbered question.**

Participant Initials: __1____ See below for Visit Record
Patient ID: _____2_____

CONTACT INFORMATION

This information should NOT be entered into Velos or disclosed outside your local NEPTUNE site.

Personal Details – *for shadow chart only*

First Name: 3 Middle Name: 4

Last Name: 5 SSN: 6

Contact Information

Address 1: 7 Address 2: 8

City: 9 County: 10

State/Province: 11 Zip/Postal: 12

Country: 13 Email: 14

Home Ph#: 15 Work Ph#: 16

Next of Kin Contact Information

First Name: 17 Last Name: 18

Address: 19 City: 20

State/Province 21 Zip/Postal: 22

Country: 23 Phone #: 24

Date each COMPLETED study visit in which you have confirmed the above information:

Visit Number	Date	No Change	Information Updated *(use a blank form)*
2	25	26	27
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			

28 Coordinator Name (Print): _____ Date: _____

29 Coordinator Signature: _____

30 *Make copies as needed*

Form 2B Contact Information Worksheet V3 Feb-2012 Page 1 of 1

16.C.5.a. *Contact Information Worksheet Reference*

This information should NOT be entered into Velos or disclosed outside your local NEPTUNE site.

Header

1 Please enter the participant's initials.

2 Please enter the Velos ID (e.g. 004021)

Personal Details

3 Please enter the participant's first name (and any nicknames you may wish to recall)

4 Please enter the participant's middle name.

5 Please enter the participant's last name.

6 Please enter the participant's social security number

The participant's SSN should NOT be entered into Velos

7 Please enter the participant's home (street) address.

8 Please enter the participant's secondary street address (apartment, building, etc).

9 Please enter the city where the participant lives.

10 Please enter the county where the participant lives.

11 Please enter the participant's state or province.

12 Please enter the participant's zip or postal code.

13 Please enter the participant's country.

14 Please enter the participant's email address.

15 Please enter the participant's home or cell phone number (ask for the best form of contact).

16 If the participant is willing to provide a work phone number, please document, otherwise request a secondary phone number where they can be reached or indicate UNK.

***NEXT OF KIN CONTACT INFORMATION WILL NOT BE ENTERED INTO VELOS. THIS WILL BE MAINTAINED IN THE PARTICIPANTS SHADOW CHART AND ONLY USED FOR LAST RESORT COLLECTION OF FOLLOW UP INFORMATION.**

Next of Kin Details

17 Please ask the participant for a next of kin contact and enter their first name.

18 Please enter the next of kin contact last name.

19 Please enter the next of kin address.

20 Please enter the next of kin city.

21 Please enter the next of kin state or province.

22 Please enter the next of kin zip or postal code.

23 Please enter the next of kin country.

24 Please enter the next of kin contact phone number.

25 Please document that Form 2B has been reviewed and updated at every study visit by indicating the date beside the respective visit number.

26 Please document if there has been no change to the contact information or the next of kin contact information by marking an “X” in this box, next to the corresponding study visit.

27 If there had been an update to the contact information or the next of kin contact information, please indicate with an “X” in this box, in the corresponding row for the study visit.

28-29:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

30 If an update is needed, as indicated by the “X” in space 27, please use a clean Contact Information Worksheet (Form 2B) and enter the new information.

This new Contact Information Worksheet should be placed *on top* of the previous information, and all documents maintained for the course of the study.

16.C.6. Form 3 Healthcare Provider Worksheet

***Please see the reference below for a complete description of each numbered question.**

Participant Initials: __1___ Visit Date (V1): ___2_____

Patient ID: _____3_____

HEALTHCARE PROVIDER INFORMATION

Review and update, as necessary, every visit.

(Local Data entry: enter the date of the current visit in the "Visit Date" field in Velos)

	4 Healthcare Provider Type (check only one)						Primary Care
5	Active, effective:						Nephrologist
6	Inactive, effective:						Other:
Last Name		First Name		MI		email:	
7		8		9		10	
Address: 11				City: 12			
State/Province: 13				Zip/Postal Code: 14			
Country 15		Phone 16		Fax 17			

	Provider Type (check only one)						Primary Care
	Active, effective:						Nephrologist
	Inactive, effective:						Other:
Last Name		First Name		MI		email:	
Address:				City:			
State/Province:				Zip/Postal Code:			
Country		Phone		Fax			

	Provider Type (check only one)						Primary Care
	Active, effective:						Nephrologist
	Inactive, effective:						Other:
Last Name		First Name		MI		email:	
Address:				City:			
State/Province:				Zip/Postal Code:			
Country		Phone		Fax			

23 *Make copies as needed*

Form 3 Healthcare Provider Worksheet V3 Feb-2012 Page 1 of 2

Participant Initials: __1___ Visit Date (V1): ___2_____

Patient ID: _____3_____

Date each COMPLETED study visit in which you have confirmed the above information:

Visit Number	Date	No Change	Information Updated *(use a blank form)*
2	18	19	20
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			

21 Coordinator Name (Print): _____ Date: _____

22 Coordinator Signature: _____

23 *Make copies as needed*

16.C.6.a. *Form 3 Healthcare Provider Worksheet Reference*

Header

1 Please enter the participant's initials.

2 Please enter the study visit date.

3 Please enter the Velos ID (e.g. 004021)

Healthcare Provider Details

4 Please check the provider type according to the study participant. Only check one selection.

We have included this check box in order to keep track of participant's current healthcare providers. We would like to have a record of all healthcare providers treating the participant while they are on study. At baseline, please enter only the active providers.

5 Please indicate the date which the provider became "active" as a caregiver for the participant, according to the participant.

6 If a participant indicates a healthcare provider is no longer "active"; document the date, according to the participant.

7 Please enter the provider's first name.

8 Please enter the provider's last name.

9 Please enter the provider's middle initial

10 Please enter the provider's email address. If unavailable, please enter UNK.

11 Please enter the provider's street address (including suite, building, etc).

12 Please enter the provider's city of practice.

13 Please enter the participant's state or province.

14 Please enter the participant's zip or postal code.

15 Please enter the participant's country.

16 Please enter the provider's phone number.

17 Please enter the provider's fax number.

18 Please document that Form 3 has been reviewed and updated at every study visit by indicating the date beside the respective visit number.

19 Please document if there has been no change to the Healthcare Provider Worksheet by marking an "X" in this box, next to the corresponding study visit.

20 If there has been an update to the Healthcare provider information, please indicate with an "X" in this box, in the corresponding row for the study visit.

21-22:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

23 If an update is needed, as indicated by the "X" in space 20, please use a clean Healthcare Provider Worksheet (Form 3) and enter the new information.

This new Healthcare Provider Worksheet should be placed *on top* of the previous information, and

all documents maintained for the course of the study.

16.C.7. Form 4A Baseline Participant Information Worksheet

***Please see the reference below for a complete description of each numbered question.**

Participant Initials: __1___ Visit Date (V1): ___2_____

Patient ID: _____3_____

BASELINE PARTICIPANT INFORMATION

Demographic Data

4 **Is English participant's primary language?**		Yes		No (*See Below)			
5 *If no, specify language:*							
6 *If no, specify proficiency in English:*		Excellent		Limited		Elementary	None

7

Ethnic background: (Check only one)		Hispanic or Latino (*See Below)		
		Not Hispanic or Latino		Not Reported
If Hispanic or Latino (Check all that apply):		Mexican American or Mexican		Dominican
8		Central American		Spaniard or Portuguese
		South American		Other (specify)
		Puerto Rican	9	
		Cuban		Don't Know

10

Racial background: (Check all that apply)		American Indian/Alaskan Native		Asian/Asian American (*See Below)
		Black/African American (*See Below)		Native Hawaiian/Other Pacific Islander
		White/Caucasian		Not Reported

If Asian/Asian American (Check all that apply):		Chinese		East Indian/South Asian (e.g. Indian, Pakistani)
11		Japanese	■	
		Filipino		Korean
		Southeast Asian (e.g. Vietnamese, Thai, Cambodian, Laotian, Burmese)		Other (specify)
	■		12	
				Don't Know
If Black/African American (Check all that apply):		American		African (specify)
13		Haitian		
		Jamaican		Cuban
		Peurto Rican		Dominican
		Other Caribbean Island		Central/South American
		Other (specify)		Don't Know
	14			

Socio-Economic Status

15

Current employment status: (Check all that apply)		Employed part-time		Employed full-time
		*Temporarily laid off/on strike		*On temporary medical leave
		*Permanently disabled		*Retired, not currently working
		Retired, new career/working		Full-time home maker
16		*Unemployed		Not Applicable

If not currently employed, last employed:	Month:	17	Year:

Form 4A Baseline Participant Info Worksheet v3 Feb-2012 Page 1 of 4

Participant Initials: __1___ Visit Date (V1): ___2_____

Patient ID: _____3_____

Primary type of work: (*Check only one*) 18		
	☐	Professional, executive occupation, business owner
	☐	Manager, technical occupation
	☐	Clerical, sales, administrative support occupation, technician
	☐	Skilled labor (e.g. certified electrician, carpenter, welder)
	☐	Semi-skilled labor (e.g. construction help, mechanic's help)
	☐	Unskilled labor (e.g. porters, bell hops, manual labor)
	☐	Homemaker
	☐	Other (specify) 19
	☐	Not Applicable

Current student status: (*Check all that apply*) 20				
	☐	Full-time	☐	Part-time
	☐	Home Schooled	☐	Not enrolled (age eligible)
	☐	Not enrolled (age ineligible / too young)	☐	Receiving special education services
			☐	Not Applicable

Highest grade/level of school completed by participant: (*Check only one*) 21				
	☐	Too young	☐	Pre-school
	☐	Kindergarten	☐	1st grade
	☐	2nd grade	☐	3rd grade
	☐	4th grade	☐	5th grade
	☐	6th grade	☐	7th grade
	☐	8th grade	☐	9th grade
	☐	10th grade	☐	11th grade
	☐	12th grade	☐	High school diploma or equivalent
	☐	2-year associates degree/certificate	☐	4-year college degree
	■		☐	Graduate level diploma (MD, PhD, PharmD, etc.
	☐	Master's level diploma	■	

Has participant ever been held back a grade: (*Check only one*) 22				
	☐	Yes	☐	No
	☐	Don't know	☐	Do not wish to answer

Highest grade/level of school completed by mother (or primary caregiver/guardian): (*Check only one*) 23				
	☐	Pre-school	☐	Kindergarten
	☐	1st grade	☐	2nd grade
	☐	3rd grade	☐	4th grade
	☐	5th grade	☐	6th grade
	☐	7th grade	☐	8th grade
	☐	9th grade	☐	10th grade
	☐	11th grade	☐	12th grade
	☐	High school diploma or equivalent	■	2-year associates degree / certificate
	■		☐	Master's level diploma
	☐	4-year college degree	☐	Don't know
	☐	Graduate Level Diploma (MD, PhD, PharmD, etc.)	☐	Not Applicable
	■			

Participant Initials: __1___ Visit Date (V1): ____2_____

Patient ID: _____3_____

Highest grade/level of school completed by father (or second caregiver/guardian): (*Check only one*) 24				
	☐	Pre-school	☐	Kindergarten
	☐	1st grade	☐	2nd grade
	☐	3rd grade	☐	4th grade
	☐	5th grade	☐	6th grade
	☐	7th grade	☐	8th grade
	☐	9th grade	☐	10th grade
	☐	11th grade	☐	12th grade
	☐	High school diploma or equivalent	☐	2-year associates degree / certificate
	☐	4-year college degree	☐	Master's level diploma
	☐	Graduate Level Diploma (MD, PhD, PharmD, etc.)	☐	Don't know
	☐		☐	Not Applicable

Current or Expected Gross Annual Household Income: (*Check only one*) 25						
	☐	$0 - $19,999	☐	$20,000 - $39,999	☐	$40,000 - $59,999
	☐	$60,000 - $79,000	☐	$80,000 - $99,000	☐	$100,000 +
	☐	Do not wish to answer	☐	Don't know		

Number of adults (18 and older) in the same household:	26	**Number of children (under 18) in the same household:**	27

Healthcare Utilization

	Don't know	**# of Times**
During the past 6 months, how many times has the participant received care in an Emergency Room in a Hospital?	28	
During the past 6 months, how many times has the participant been seen by a healthcare provider for well/checkup visits (Do not include this study visit or dental visits)?	29	
During the past 6 months, how many times has the participant been seen by a healthcare provider for sick/injury visits (Do not include this study visit, dental visits or times when hospitalized overnight)?	30	
During the past 6 months, has the participant been hospitalized (apart from being born)?	31	
AND total # of days:		32

Health Insurance

Participant currently has: (*Check all that apply*) 33				
	☐	Private health insurance plan	☐	Medicare/Medicaid
	☐	Military/VA	☐	None
	☐	Other type(s) of health insurance (specify)		
		34		

Birth History

Birth weight:	35	Don't know	36	37	*lbs	38	grams	39	*oz (if lbs)
Birth length:	40	Don't know	41	42	Inches		43	cm	
Gestational age:	44	Don't know	45	weeks					

Participant Initials: __1___ Visit Date (V1): ___2_____

Patient ID: _____3_____

Born in the Hospital: 46		Yes		No		Don't know				
How Delivered: 47		Vaginal birth		C-section		Don't know				
Were you: 48		Full Term (>= 36 weeks)		*Premature (< 36 weeks)		Don't know				
**If premature, # of weeks:*		49		Weeks		Don't know				
Part of a multiple birth (twin, triplet, etc.): 50				Yes		No		Don't know		
Immediately after birth, spent time in the NICU or ICU: 51				Yes		No		Don't know		
Immediately after birth, have any kidney problems: 52				Yes		No		Don't know		
53 **Time spent in the hospital after delivery:**		Don't know		Not applicable				Days		

Age of biological mother at birth:		Don't know	54	years	
Racial background of biological mother *(Check all that apply):* 55		American Indian/Alaskan Native		Asian/Asian American	
		Black/African American		Hispanic/Latina	
		Native Hawaiian/Other Pacific Islander		White/Caucasian	
		Unknown		Other (specify)	
			56		

Age of biological father at birth:		Don't know	57	years	
Racial background of biological father *(Check all that apply):* 58		American Indian/Alaskan Native		Asian/Asian American	
		Black/African American		Hispanic/Latina	
		Native Hawaiian/Other Pacific Islander		White/Caucasian	
		Unknown		Other (specify)	
			59		

Social History

Current smoker: 60		Yes (*See Below)		No		
Previous Smoker 61		Yes (*See Below)		No		
**If Yes for current or previous smoker:*	# of packs smoked a day	62				(there are 20 cigarettes in 1 pack)
	# of years smoking	63				
Pipe or Cigar Use: 64		Yes		No		
Passive smoker (do any of the people who live in the participant's primary household smoke cigarettes, cigars, cigarillos, little cigars or pipes? 65		Yes		No		

Other Drug Use: 66		Yes (specify)	67				No	
Alcohol Use 68 ***(Check only one)***		Daily		3-4 times/week			1-2 times/week	
		1-2 times/month		Less than once/month			None	

69 Coordinator Signature: _____ Date: _____

70 Coordinator Name (Print): _____

Form 4A Baseline Participant Info Worksheet v3 Feb-2012 Page 4 of 4

16.C.7.a. *Form 4A Baseline Participant Information Worksheet Reference*

Header

1 Please enter the participant's initials.

2 Please enter the study visit date.

3 Please enter the Velos ID (e.g. 004021)

Demographic Data

4 Please check "Yes" or "No.". If "No" is checked please answer questions 5 and 6.

5 If "No" is checked, please write in the participant's primary language.

6 If "No" is checked, ask the participant's English proficiency and check the coordinating box.

Excellent: Able to use the language fluently and accurately.

Limited: Able to satisfy routine social demands and limited work requirements.

Elementary: Able to satisfy routine travel needs and minimum courtesy requirements.

None: No understanding of English.

7 Provide ethnicity choices to the participant and check the box that corresponds with the participant's response.

This answer should be their self-reported ethnicity. Check only one. If "Hispanic or Latino" is checked, please answer question 8

8 If "Hispanic or Latino" is checked, please ask participant to specify origin. More than one box can be checked.

9 If "Other" is checked, please ask participant to specify.

10 Provide race choices to the participant and check the box accordingly. This should be the participant's self-reported race. More than race can be checked

11 If "Asian-American" is checked, please specify origin. More than one box can be checked.

12 If "Other" is checked, please ask participant to specify the country.

13 If "Black/African American" is checked, please specify origin. More than one box can be checked.

14 If "Other" is checked, please ask participant to specify the country and record it in the provided space (If they do not know the country enter UNK).

Socio-Economic

15 Provide employment status choices to the participant and check the box accordingly. More than one option may be checked.

16 If participant is not currently employed, please ask them to specify the month and year they were employed last.

17 Enter the month and year of last employment in the spaces provided.

18 Provide primary work type choices to the participant and check the box accordingly. If the participant previously stated that they were unemployed please check N/A

19 If the participant specifies another type of work not listed, please record here.

20 If participant is enrolled in school, provide student status choices and check the appropriate box. More than one option may be checked.

21 Check the box with the highest level of education achieved by the participant. Check only one option.

22 Please check box "Yes," "No," "Don't Know," or "Do not wish to Answer."

23 Please check the correct box according to participant account. If the participant is not sure please check "Don't Know." Check only one option.

24 Please check the correct box according to participant account. If the participant is not sure please check "Don't Know" and if the participant does not have a second caregiver please check "Not Applicable." Check only one option.

25 Please enter the participant's gross annual income. If the participant does not have a gross annual income, enter the gross annual income of the participant's primary residence. If participants ask why you are collecting this information, please refer to the following suggested language:

"*While this is a kidney study, researchers are interested in what can affect your health. Just as race, ethnicity and stress level have been linked to health, researchers have found links between economic status and health outcomes. Remember, this information will not be shared outside of the research staff, and it will not have your name on it. We want to protect your privacy, as well as collect information desired by NEPTUNE researchers."*

26 Consult with the participant and record the number of adults, age 18 or older, living in their primary residence.

27 Consult with the participant and record the number of children, under age 18, living in their primary residence.

Healthcare Utilization

28 Please enter the # of times the participant has received care in an emergency room over the last 6 months (enter 0 if they have not received care in an emergency room over the last 6 months). Check "Don't Know" if the participant cannot recall.

29 Please enter the # of times the participant has been seen by any healthcare provider for well/checkup visits over the last 6 months (enter 0 if they have not been seen over the last 6 months). Do not include dental office visits in this calculation. Check "Don't Know" if the participant cannot recall.

30 Please enter the # of times the participant has been seen by a healthcare provider for sick/injury visits over the last 6 months (enter 0 if they have not been seen for a sickness or injury over the last 6 months). Do not include this visit, overnight hospitalizations or dental visits in the calculation. If the participant cannot recall, check "Don't Know."

31 Please check "Don't Know" if participant can't recall. Otherwise please enter the number of times they were hospitalized (enter 0 if the participant has not been hospitalized in the last 6 months).

32 Please sum and enter the total number of days the participant was hospitalized in the pasat 6 months.

Health Insurance

33 Please check all that apply.

34 If and "Other type of health insurance" is indicated, please ask the participant to specify and record here.

Birth History

35 Please enter in the participant's birth weight according to participant or parent account.

36 If the participant cannot recall their birth weight, check "Don't Know" and ask the participant to gather this information if possible, and bring it in at their next appointment. You can update this

field at a later time if more information is obtained.

37 Please enter the birth weight in pounds, if known.

38 Please enter the birth weight in grams, if known.

39 Please enter the birth weight ounces, if known.

40 Please enter in the participant's birth length according to participant or parent account.

41 If the participant cannot recall their birth length, check "Don't Know" and ask the participant to gather this information if possible, and bring it in at their next appointment. You can update this field at a later time if more information is obtained.

42 Please enter the birth length in inches, if known.

43 Please enter the birth length in centimeters, if known.

44 Please enter in the participant's gestational age in weeks (the time from conception to birth) according to participant or parent account. If the participant cannot recall their gestational age, check "Don't Know" and ask the participant to gather this information if possible, and bring it in at their next appointment. You can update this field at a later time if more information is obtained.

45 Please enter the gestational age in weeks, if known.

46 Please check "Yes," "No" or "Don't Know" to indicate if a participant was born in a hospital. Again, if the participant can obtain this information for their next visit, please update this field with the correct answer.

47 Please check the appropriate box.

48 Please check the appropriate box.

49 If "Premature" was checked above, please ask them to give the number of weeks early their birth was. Again, if the participant does not currently have this information, ask them to obtain it if possible. If the information cannot be obtained, please check "Don't Know."

50 Please check "Yes," "No" or "Don't Know."

51 Please check "Yes," "No" or "Don't Know." (ICU is Intensive Care Unit and NICU is Neonatal Intensive Care Unit)

52 Please check "Yes," "No" or "Don't Know."

53 Ask the participant to provide the total number of days they spent in the hospital after delivery. If the participant was not born in the hospital please check "Not Applicable." If the participant does not know the exact amount of time spent please check "Don't Know."

54 Please enter in the age. If participant cannot provide age, please ask them to attempt to obtain this information and bring it in at the next study visit.

55 Please check the appropriate box. More than one box can be checked. If participant cannot provide race, please ask them to attempt to obtain this information and bring it in at the next study visit.

56 If other is checked, please ask the participant to specify.

57 Please enter in the age. If participant cannot provide age, please ask them to attempt to obtain this information and bring it in at the next study visit.

58 Please check the appropriate box. More than one box can be checked. If participant cannot provide race, please ask them to attempt to obtain this information and bring it in at the next study visit.

59 If other is checked, please ask the participant to specify.

Social History

60 This question refers to cigarettes. Please answer "Yes" or "No" to the question of current smoker. If "Yes" is checked for current smoker, do not check anything for previous smoker and answer questions 62 and 63.

61 This question refers to cigarettes. Please answer "Yes" or "No" to the question of previous smoker and complete questions 62 and 63.

62 If "Yes" is checked for either previous or current smoker, please ask the participant to estimate the number of packs smoked per day.

63 If "Yes" is checked for either previous or current smoker, please ask the participant to estimate the number of years that they have (or they did) smoke.

64 Please check "Yes" or "No."

65 Please check "Yes" or "No."

66 Please check "Yes" or "No."

67 If "Yes" is checked, please ask them to specify the drug(s).

68 Please as the participant to specify alcohol use frequency. If they do not consume alcohol, please check none. Only check one box.

69-70:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.8. Form 4B Baseline Family History Worksheet

***Please see the reference below for a complete description of each numbered question.**

Participant Initials: __1___ Visit Date (V1): ____2_____

Patient ID: _____3_____

BASELINE FAMILY HISTORY INFORMATION

Family History of Kidney Disease

Does participant have a family history of kidney disease? 4		Yes*		No		Don't know
Has participant's biological mother / father been diagnosed with kidney disease? *(circle one – make add'l copies of this form if necessary)* 5		Yes*		No		Don't know

**If yes, please specify disease (Only check one):* 6

	Acute Interstitial Nephritis		Henoch-Schoenlein Purpura (HSP)		Nephrotic Syndrome (unspecified or unknown)
	Acute Renal Failure		Hypertensive Nephropathy (Hypertensive Nephrosderosis)		Polycystic Kidney Disease
	Acute Tubular Necrosis		IgA-Nephritis		Post-infectious Glomerulonephritis (Infection-related Glomerulonephritis)
	Alport		Infectious/Complement Mediated Glomerulonephritis		Rapidly Progressive Renal Failure
	Amyloidosis		Membrano-proliferative Glomerulonephritis		Renal Dysplasia
	Atheroembolic Disease		Membranous Glomerulopathy (Membranous Nephropathy)		Sarcoidosis
	Chronic Interstitial Nephritis		Minimal Change Disease (Nil Disease)		Thin Basement Membrane Nephropathy
	Chronic Renal Failure (unspecified or unknown)		Monoclonal Gammopathy (Multiple Myeloma)		Thin Basement Membrane Nephropathy
	Diabetic Nephropathy		Nail Patella		Thrombotic Thrombocytopenic Purpura (TTP)
	Focal and Segmental Glomerulosclerosis (FSGS)		Nephritis		Vasculitis
	Hemolytic-Uremic Syndrome (HUS)		Unknown		Other – Specify below*

7 **Other*:** _____

**If additional kidney diseases were diagnosed, please list them here:*

8_____

Please specify age of onset 9		Years			Don't know
Is there an archived kidney biopsy? 10		Yes		No	Don't know
Is this person on Dialysis? 11		Yes		No	Don't know

Form 4B Baseline Family History Worksheet v3 Feb-2012 Page 1 of 4

Participant Initials: __1___ Visit Date (V1): ____2_____

Patient ID: _____3_____

How many siblings does the participant have with at least one common parent? 12		1		5		9
		2		6		10
		3		7		None
		4		8		Don't Know

Have any of these siblings been diagnosed with kidney disease? 13		Yes		No		Don't Know

How many biological children does the participant have? 14		1		5		9
		2		6		10
		3		7		None
		4		8		Don't Know

Have any of these children been diagnosed with kidney disease? 15		Yes		No		Don't Know

16:

*IF MORE THAN ONE SIBLING OR CHILD HAS BEEN DIAGNOSED, PLEASE MAKE ADDITIONAL COPIES OF THE FOLLOWING PAGE (PAGE 3) AND COMPLETE FOR UP TO 4 SIBLINGS OR 4 CHILDREN. PLEASE BE SURE TO INDICATE WHICH SIBLING OR CHILD THE PAGE IS FOR BY CHECKING THE APPROPRIATE BOX AT THE TOP OF THE PAGE.

Participant Initials: __1___ Visit Date (V1): ____2_____

Patient ID: _____3_____

Sibling #	17		1		2		3		4
Child #	18		1		2		3		4

Please specify disease (Only check one): 19

	Acute Interstitial Nephritis		Henoch-Schoenlein Purpura (HSP)		Nephrotic Syndrome (unspecified or unknown)
	Acute Renal Failure		Hypertensive Nephropathy (Hypertensive Nephrosclerosis)		Polycystic Kidney Disease
	Acute Tubular Necrosis		IgA-Nephritis		Post-infectious Glomerulonephritis (Infection-related Glomerulonephritis)
	Alport		Infectious/Complement Mediated Glomerulonephritis		Rapidly Progressive Renal Failure
	Amyloidosis		Membrano-proliferative Glomerulonephritis		Renal Dysplasia
	Atheroembolic Disease		Membranous Glomerulopathy (Membranous Nephropathy)		Sarcoidosis
	Chronic Interstitial Nephritis		Minimal Change Disease (Nil Disease)		Thin Basement Membrane Nephropathy
	Chronic Renal Failure (unspecified or unknown)		Monoclonal Gammopathy (Multiple Myeloma)		Thin Basement Membrane Nephropathy
	Diabetic Nephropathy		Nail Patella		Thrombotic Thrombocytopenic Purpura (TTP)
	Focal and Segmental Glomerulosclerosis (FSGS)		Nephritis		Vasculitis
	Hemolytic-Uremic Syndrome (HUS)		Unknown		Other – Specify below*

20 **Other*:** _____

**If additional kidney diseases were diagnosed, please list them here:*

21 _____

Please specify age of onset	22		Years		Don't know		
Is there an archived kidney biopsy?	23		Yes		No		Don't know
Is this person on Dialysis?	24		Yes		No		Don't know

For additional sibling(s) / child(ren) please copy this page and complete

Participant Initials: __1___ Visit Date (V1): ____2_____

Patient ID: _____3_____

Family History of Diabetes

Does participant have a family history of diabetes?	25		Yes		No		Don't know
**If yes, check all that apply:*	26		Biological Mother			
			Biological Father			
			Sibling(s) *(with at least 1 common parent)*			
Number of Siblings with diabetes?	27		Total		Don't Know	
Number of biological children with diabetes?	28		Total		Don't Know	

Family History of Hypertension

Does participant have a family history of hypertension?	29		**Yes**		**No**		**Don't know**
**If yes, check all that apply:*	30		Biological Mother			
			Biological Father			
			Sibling(s) *(with at least 1 common parent)*			
Number of Siblings with hypertension?	31		Total		Don't Know	
Number of biological children with hypertension?	32		Total		Don't Know	

33 Coordinator Signature: _____ Date: _____

34 Coordinator Name (Print): _____

16.C.8.a. *Form 4B Baseline Family History Worksheet Reference*

Header

1 Please enter the participant's initials.

2 Please enter the study visit date.

3 Please enter the Velos ID (e.g. 004021)

Family History of Kidney Disease

4 Please check "Yes", "No" or "Don't Know."

5 Please check "Yes," "No" or "Don't Know." If yes, circle "Mother" or "Father" to indicate which biological parent has been affected by kidney disease, and if necessary, make an additional copy of the sheet (i.e., both parents affected by kidney disease).

6 If "Yes" is checked, please provide the list of diseases to the participant and check the appropriate box (Only check one box). Please confirm with the patient that the disease was a diagnosis by a medical professional. If the participant is not sure of their mother/father's diagnosis, please check "Unknown." If the disease given by the participant is not listed, please check "Other" and write in the disease name.

Acute Interstitial Nephritis: Nephritis affecting the interstitium of the kidneys and occurring suddenly.

Acute Renal Failure: Rapid loss of kidney function.

Acute Tubular Necrosis: Rapid death of tubular cells (tubule of the kidney). Can present with Acute Renal Failure.

Alport: Genetic disorder characterized by glomerulonephritis, endstage renal disease, and hearing loss.

Amyloidosis: Any condition where amyloid proteins are abnormally deposited in organs and/or tissues.

Atheroembolic Disease: An inflammatory reaction in the small blood vessels of the kidneys.

Chronic Interstitial Nephritis: An ongoing form of nephritis affecting the interstitium of the kidneys.

Chronic Renal Failure (Unspecified/Unknown): Progressive loss of renal function over a period of months or years with no specified cause.

Diabetic Nephropathy: Kidney disease/damage resulting from diabetes complications.

Focal and Segmental Glomerulosclerosis (FSGS): A disease that attacks the kidney's filtering system causing scarring of the tissue.

Hemolytic-Uremic Syndrome (HUS): A syndrome characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. Primarily occurring in infancy and children.

Henoch-Schoenlein Purpura (HSP): A form of blood vessel inflammation that affects the capillaries in the skin and often times the kidneys.

Hypersensitive Nephropathy (Hypertensive Nephrosclerosis): Damage to the kidney due to chronic high blood pressure.

Iga Nephritis: A form of glomerulonephritis. Also known as Berger's Disease.

Infectious/Compliment Mediated Glomerulonephritis: Acute glomerulonephritis mediated by an infection.

Membrano-Proliferative Glomerulonephritis: Glomerulonephritis caused by deposits in the kidney glomerular mesangium and basement membrane thickening.

Membranous Glomerulopathy: A kidney disorder that involves changes and inflammation of the

structures inside the kidney that help filter waste.

Minimal Change Disease (Nil Disease): Nephrotic Syndrome that reveals little or no change in the structure of the glomeruli or surrounding tissues when the kidneys are biopsied.

Monoclonal Gammopathy: Condition where abnormal protein is found in the blood and may progress over decades to other disorders. Also known as MGUS.

Nail Patella: A genetic disorder characterized by small poorly developed nails and kneecaps. Persons with this syndrome may also develop kidney disease. Also referred to as Iliac Horn Syndrome, Hereditary Onychoostedysplasia, Fong Disease, or Turner-Kiser Syndrome.

Nephritis: Inflammation of the kidneys.

Nephrotic Syndrome (Unspecified): A non-specific disorder in which the kidney's are damaged and leaking large amounts of protein.

Polycystic Kidney Disease: A cystic genetic disorder of the kidneys. Also known as PKD or PCKD.

Post-Infectious Glomerulonephritis (Infection Related Glomerulonephritis): Glomerulonephritis as a result of an infection.

Rapidly Progressing Renal Failure: Rapid loss of kidney function which occurs over a few weeks to a few months.

Renal Dysplasia: Abnormal cellular differentiation of the renal tissue.

Sarcoidosis: A multi-system inflammatory disease characterized by small inflammatory nodules. Also known as Besnier-Boeck Disease.

Thin Basement Membrane Nephropathy: Disease characterized by a thinning of the basement membrane of the glomeruli in the kidneys. Also known as Benign Familial Hematuria.

Thrombotic Thrombocyopenic Purpura (TTP): Rare disease of the blood-coagulation system, causing extensice microscopic thromboses to form in blood vessels throughout the body. Also known as Moschcowitz Syndrome.

Vasulitis: Disorder that is characterized by the inflammatory destruction of blood vessels.

7 If "Other" is indicated, please record the affected family member's disease.

8 If afflicted family member was diagnosed with additional kidney diseases, please list them on this line, separated by commas. Only one box should be checked for question 6.

9 Please ask them to specify the age of onset (of afflicted family member's disease)

10 Please ask them if the afflicted family member an archived kidney biopsy.

11 Please ask them if the afflicted family member is on dialysis.

12 Please check the number of siblings the participant has with at least one common parent. If participant has none, please check "None" and if participant does not know, please check "Don't Know".

13 Please check "Yes," "No" or "Don't Know". Check "Yes" if ANY of the siblings have been diagnosed with kidney disease and "No" if none have been diagnosed.

14 Please check the number of biological children that the participant has. If the participant has none, please check "None" and if the participant does not know, please check "Don't Know".

15 Please check "Yes," "No" or "Don't Know". Check "Yes" if ANY of the children have been diagnosed with kidney disease and "No" if none have been diagnosed.

16 If more than one sibling or child has been diagnosed with kidney disease, please make additional copies of Page 3 and complete for up to 4 siblings, or 4 children. Please indicate which sibling or

child this for by checking the appropriate box at the top of the page.

17 If "Yes" is checked, please specify the sibling affected by checking sibling 1, 2, 3, or 4. For each diagnosed sibling, please copy and complete page 3.

For example: If you only have one diagnosed sibling you would only have one copy of page 3 and you would have sibling 1 checked. If you had two diagnosed siblings you would have two copies of page 3 and would have sibling 1 checked on one of the copies (providing information about sibling 1) and sibling 2 checked on the second copy (providing information about sibling 2).

18 If "Yes" is checked, please specify the child affected by checking child 1, 2, 3, or 4. For each diagnosed sibling, please copy and complete page 3. See above for example.

19 If "Yes" is checked, provide the list of diseases to the participant and check the appropriate box (Only check one box per afflicted family member). Please confirm with the patient that the disease was a diagnosis by a medical professional. If the participant is not sure of their sibling or child's diagnosis, please check "Unknown.:

20 If "Other" is indicated, please record the affected family member's disease.

21 If afflicted family member was diagnosed with additional kidney diseases, please list them on this line, separated by commas. Only one box should be checked for question 6.

22 Please ask them to specify the age of onset (of afflicted family member's disease)

23 Please ask them if the afflicted family member an archived kidney biopsy.

24 Please ask them if the afflicted family member is on dialysis.

Family History of Diabetes

25 Please check "Yes", "No" or "Don't Know." Confirm with the patient that diabetes was a diagnosis by a medical professional.

26 If "Yes," check all that apply.

27 Indicate the total number of siblings with diabetes, if unknown, check "Don't Know".

28 Indicate the total number of children with diabetes, if unknown, check "Don't Know".

Family History of Hypertension

29 Please check "Yes", "No" or "Don't Know." Confirm with the patient that hypertension was a diagnosis by a medical professional.

30 If "Yes," check all that apply.

31 Indicate the total number of siblings with hypertension, if unknown, check "Don't Know".

32 Indicate the total number of children with hypertension, if unknown, check "Don't Know".

33-34:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.9. Form 4C Baseline Clinical Information Worksheet

***Please see the reference below for a complete description of each numbered question.**

Participant Initials: __1___ Visit Date (V1): ___2_____

Patient ID: _____3_____

BASELINE CLINICAL INFORMATION

Date of initial presentation of proteinuria/nephrotic syndrome: 4 (please estimate month and year if not known)		**Month**		**Year**

Height of participant prior to onset of Kidney Disease: 5		**Height**	*Circle one*	
			inches	**cm**

Weight of participant prior to onset of Kidney Disease: 6		**Weight**	*Circle one*	
			pounds	**kg**
			Don't know	

Nephrotic Syndrome Treatment History

Has participant ever received treatment for Nephrotic Syndrome? 7		**Yes***		**No**
			Don't Know	
*If Yes, please check all that apply and enter estimated cumulative total duration of therapy in months for each: 8			**Not Applicable**	

	9 Therapy	Estimated Cumulative Total Duration of Therapy (in months)
	Angiotensin Converting Enzyme *(ACE Inhibitor, eg Lisinopril, Enalapril)*	
	Angiotensin Receptor Blocker *(ARB, e.g. Losartan, Irbesartan)*	
	Aldosterone Inhibitor *(Spironolactone, Eplerenone)*	
	Aliskiren	
	Cyclosporine	
	Tacrolimus (Prograf)	
	Cyclophosphamide	
	Chlorambucil	
	Levamisole	
	Oral Corticosteroids *(Prednisone, Prednisolone, Dexamethasone)*	
	Intravenous Corticosteroids *(Solumedrol, Dexamethasone)*	
	Mycophenolate Mofetil	
	Other, Specify:	

Renal Replacement Therapy History:

Has participant ever received treatment with Dialysis? 10		**Yes***		**No**
**If Yes, please provide Date started (Month/Year) and Date ended (Month/Year) for up to three treatment series.* 11			**Don't Know**	

Series		Start Date (mo/yr)		End Date (mo/yr)		Unknown
12	*1*					
	2					
	3					

Form 4C Baseline Clinical Info Worksheet v3 Feb-2012 Page 1 of 3

Participant Initials: __1___ Visit Date (V1): ___2_____

Patient ID: _____3_____

Other Medical History *(Check all that apply):* 13

		If checked, duration or year of onset				*If checked, duration or year of onset*
☐	Heart Failure		☐	Heart Arrhythmia		
☐	Stroke		☐	Peripheral Vascular Disease		
☐	Cancer		☐	Rheumatologic Disease		
	If checked, Type:			*If checked, Type:*		
☐	Hypertension		☐	Coronary Artery Disease (MI, Angina, Angioplasty, Stent, CABG)		
☐	Diabetes		☐	Thromboembolic event		
	If checked, Type:	☐ Type I		*If checked, Type: (check all that apply)*		
		☐ Type II	☐	- Deep Vein Thrombosis	☐	- Embolic Stroke
	If checked, requires insulin?	☐ Yes	☐	- Pulmonary Embolism	☐	- Renal Vein Thrombosis
		☐ No	☐	- Other:	☐	- Renal Artery Thrombosis

Any of the following Infections in the last 6 months (check all that apply): 14

☐	Peritonitis	☐	Sepsis	☐	Cellulitis / Skin Infection
☐	Pneumonia	☐	Other:		

If any infections were checked, total duration of antibiotic treatment 15				*Days*
If any infections were checked, antibiotic type used (check all that apply):	☐	Oral	☐	Parenteral (IV)
	☐	Topical	☐	Unknown

	Yes	No
Did participant ever have or does participant currently have Hepatitis? 16		
17 If Yes, Type: ☐ A ☐ B ☐ C		
Does participant have HIV? 18		
Has participant ever received one or more blood transfusion? 19		

Suffers or suffered from any of the following (Check all that apply): 20

☐	Deafness	☐	Spondyloepiphyseal Dysplasia (Schminke Disease) (inherited bone growth disorder resulting in dwarfism)
☐	Blindness	☐	Heart Anomalies: defects or abnormalities of the heart
☐	Microcephaly: med cond where head is abnormally small because the brain did not develop properly	☐	Cardiomyopathy: heart muscle becomes inflamed and does not work properly; types include dilated, hypertrophic and restrictive
☐	Mental Retardation	☐	Microcoria: congenital disease; abnormally small pupils
☐	Facial Dysmorphia (abnormality in shape/size of facial features)	☐	Male Pseudohermaphroditism: testes and XY chromosomes but appearance of external genitalia varies
☐	Polydactyly (extra fingers or toes)		

Allergies (Check all that apply): 21

	Type	Please specify allergens
☐	**Food**	
☐	**Drug**	
☐	**Environmental**	

Participant Initials: __1___ Visit Date (V1): ____2_____

Patient ID: _____3_____

	Years	Pre-pubertal
Age when participant began puberty; e.g., body hair growth (males and females), breast development (females) or deepening of the voice (males)? 22		
If exact age unknown, enter an approximation (i.e., participant's best guess) or other comment here: 23		
Age of participant's first menstrual period? 24		
	Not applicable (male)	
If exact age unknown, enter an approximation (i.e., participant's best guess) or other comment here: 25		

Clinical Symptoms

Within the last two weeks has participant had any of the following clinical symptoms? 26

	Shortness of breath		Swelling		Fever		Chest pain
	Foamy urine		Diarrhea		Nausea and/or vomit		Other

Clinical Nephrotic Exam - Vital Signs and Physical Exam

Weight: 27 kg (pounds ÷ 2.2 = kg) Height: 28 cm (inches × 2.54 = cm) Pulse: 29 beats/min

Blood Pressure:

30	Right Arm		Left Arm
	Reading:	Systolic	Diastolic
		mmHg	
Seated	1st	31	
	2nd		
	3rd		
	Average 2nd & 3rd	32	
Standing		33	

Edema Status 34

Does participant have:	Absent	Present
Periorbital / Facial Edema		
Lower Extremity Edema		
Sacral Edema		
Anasarca (extreme generalized edema)		

35 Coordinator Signature: _____ Date: _____

36 Coordinator Name (Print): _____

16.C.9.a. *Form 4C Baseline Clinical Information Worksheet Reference*

Header

1 Please enter the participant's initials.

2 Please enter the study visit date.

3 Please enter the Velos ID (e.g. 004021)

Nephrotic Syndrome Presentation

4 Please ask the participant the date of the initial presentation of their proteinuria and/or nephrotic syndrome. This will not necessarily coincide with the current presentation. Please record in month and year.

5 Please ask the participant their height prior to the onset of their kidney disease and document recording inches or centimeters. If the participant does not know, please check "Don't Know".

6 Please ask the participant their weight prior to the onset of their kidney disease and document recording pounds or kilograms. If the participant does not know, please check "Don't Know".

Nephrotic Syndrome Treatment History

7 Please check "Yes," or "No" and proceed to question 9.

8 If "Don't Know" or "Not Applicable", (if the participant has not been diagnosed with Nephrotic Syndrome to date). skip question 9.

9 If "Yes" was checked above, please check the medications used, according to participant account, and ask the participant to estimate, to the best of their ability, the total number of months they received that type of therapy (for example, if the participant received two months of cyclosporine one year and two months the following year, the total number of months of therapy received would be four). If "Other" is checked, please specify in the blank provided, including estimated duration.

Renal Replacement Therapy History

10 Please check "Yes," or "No". If "Yes" proceed to question 12.

11 If the participant does not know if they have received RRT, please check "Don't Know".

12 If "Yes" is checked for question 6, please provide the date started and date ended in months and years. If participant had only one (or only two) treatment series, please leave remaining lines blank. If treatment is ongoing, please enter start date and leave end date blank. If treatment dates are unknown, please check "Unknown."

Other Medical History

13 These items apply to the participant. Please check the box if participant currently has or has been previously diagnosed with any of the indicated diagnoses.

If checked, please ask the participant to give you the duration of time that has passed since they were diagnosed with the condition (for example, if the participant was diagnosed five years ago you would write five years) or the year of diagnosis of the condition.

For Cancer, Diabetes, Rheumatologic Disease, or Thromboembolic Event, please ask "Type" and indicate participant's response by checking the appropriate box.

14 Please check all infections participant has had in the last 6 months

Peritonitis: inflammation of the membrane which lines the abdominal cavity.

Sepsis: inflammation of the entire body (also known as SIRS) and the presence of infection.

15 If any infections were checked, please enter the time in days that they were treated in total and indicate the type of antibiotic used. Check all that apply.

16 Please check "Yes" or "No."

17 If "Yes" is checked, please select the type.

18 Please check "Yes" or "No."

19 Please check "Yes" or "No."

20 Please check all that apply.

21 Please check all that apply. If any of the allergies are checked, please ask the participant to specify the allergies and list them on the provided lines.

22 Please enter the age in years. Please check "Pre-pubertal" if puberty has not began.

23 If exact age is unknown, provide the participant's best estimate or other comment.

24 Please enter the age in years. Please check "Pre-pubertal" if participant is female and menses has not began. Please check "Not Applicable" if participant is male.

25 If exact age is unknown, provide the participant's best estimate or other comment.

Clinical Symptoms

26 Check all symptoms that apply.

Clinical Nephrotic Exam

26 Check all symptoms that apply.

27 While participant is at the study visit, please weigh them and record their weight in kilograms (Note: 1lb = 0.45359kg or pounds/2.2 = kg).

28 While participant is at the study visit, please measure their height and record it in the blank. (Note: 1in = 2.54cm).

29 While participant is at the study visit please take and record their pulse for 30 seconds.

30 While participant is at the study visit, determine from which arm blood pressured will be measured and record. Please refer to the MOP for directions on blood pressure measurement.

31 Please take and record their blood pressure in both the sitting and standing position. Take the sitting BP three consecutive times (waiting at least 30 seconds after cuff deflation) and record all three measurements.

32 Average the second and third sitting BP and record the average (this is what should be recorded in Velos).

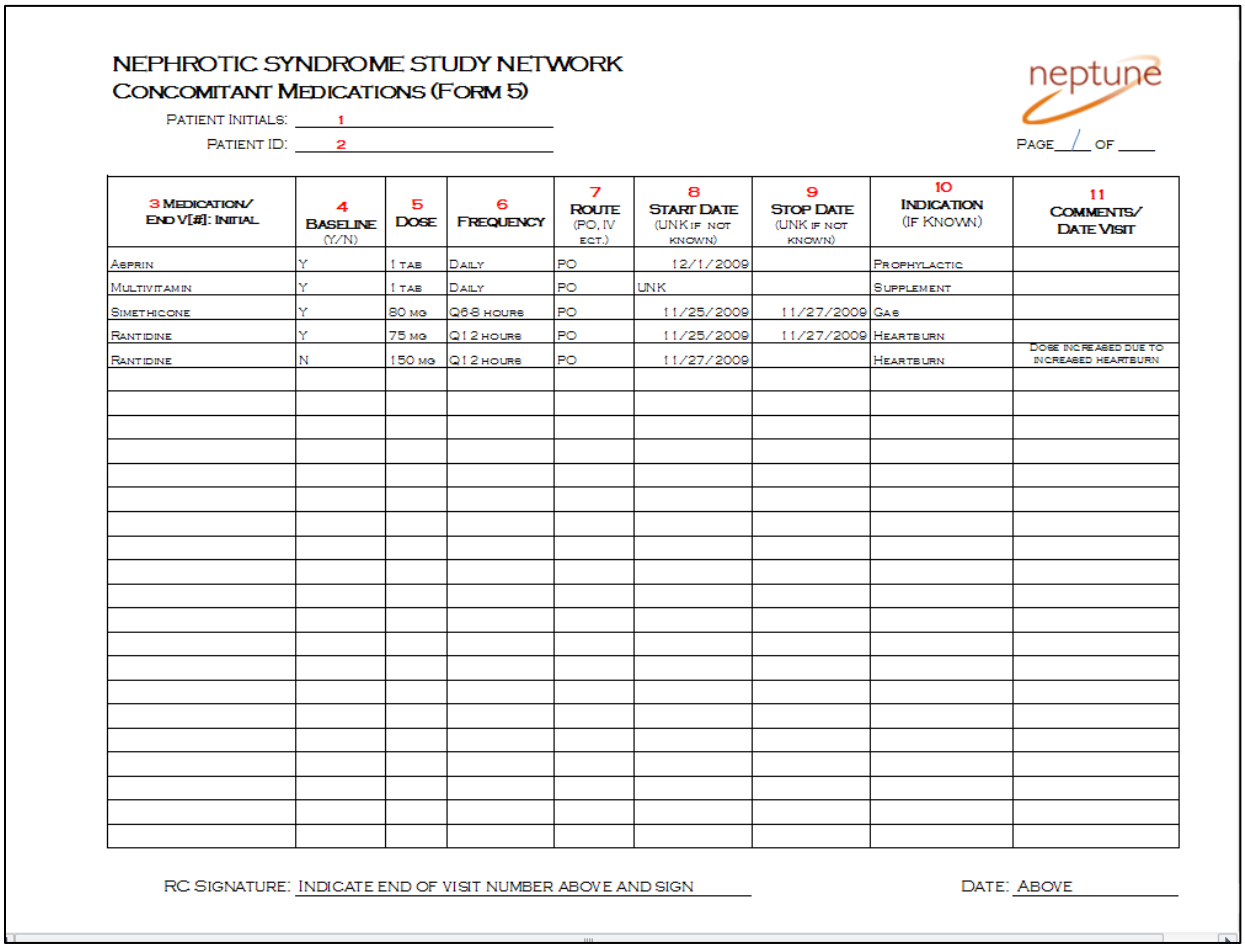
33 The standing BP should only be taken once.

34 Please examine participant at the study visit and check "Present" or "Absent" for the indicated edemae. For examination directions and edema references please refer to the MOP.

35-36:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.10. Form 5 Concomitant Medications Worksheet



NEPHROTIC SYNDROME STUDY NETWORK
CONCOMITANT MEDICATIONS (FORM 5)

PATIENT INITIALS: 1
PATIENT ID: 2

PAGE ___ OF ___

3 MEDICATION/ END V[#]: INITIAL	4 BASELINE (Y/N)	5 DOSE	6 FREQUENCY	7 ROUTE (PO, IV ECT.)	8 START DATE (UNK IF NOT KNOWN)	9 STOP DATE (UNK IF NOT KNOWN)	10 INDICATION (IF KNOWN)	11 COMMENTS/ DATE VISIT
ASPRIN	Y	1 TAB	DAILY	PO	12/1/2009		PROPHYLACTIC	
MULTIVITAMIN	Y	1 TAB	DAILY	PO	UNK		SUPPLEMENT	
SIMETHICONE	Y	80 MG	Q6-8 HOURS	PO	11/25/2009	11/27/2009	GAS	
RANTIDINE	Y	75 MG	Q12 HOURS	PO	11/25/2009	11/27/2009	HEARTBURN	
RANTIDINE	N	150 MG	Q12 HOURS	PO	11/27/2009		HEARTBURN	DOSE INCREASED DUE TO INCREASED HEARTBURN

RC SIGNATURE: INDICATE END OF VISIT NUMBER ABOVE AND SIGN DATE: ABOVE

16.C.10.a. *Form 5 Concomitant Medications Worksheet Reference*

Header

1 Record participant's initials.

2 Record Patient ID.

Medication Log

3 Under the "Medication" column please record the proper medication name.

4 Please place a "Y" in this column if the participant is taking that medication at baseline. Please place a "N" in this column if the participant was not taking that medication at baseline.

5 Under the "Dose" column please record the dose of the medication (e.g. If the participant is taking 1 baby asprin, please enter "1 tab" or "1 pill" in this column. If the participant is taking 500mg of Acetominophen please enter "500mg" in this column).

6 Under the "Frequency" column please record the frequency that the participant is taking that medication (e.g. If the participant takes a multivitamin daily please put "daily" or "QD" in this column).

7 Under the “Route” column please record the route in which the medication is taken (e.g. If the participant takes norvasc by mouth, please put “PO” or “Oral” in this column.

8 Under the “Start Date” column please enter the date that the participant started taking that medication. If the start date is unknown please enter “UNK”.

9 Under the “Stop Date” column please enter the date that the participant stopped taking that medication. If the stop date is unknown please enter “UNK”. If the medication is ongoing please leave this field blank.

10 Under the “Indication” column please enter the indication for that medication (e.g. If the participant was taking ibuprofen for pain, you would enter “pain” in this column).

11 Under the “Comments” column please place any additional comments you may have about that medication.

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.11. Form 6A-E Quality of Life Questionnaires

Participant Initials: __1____

Patient ID: _____2_____

QUALITY OF LIFE QUESTIONNAIRES

Questionnaires will be provided in paper format and are available via the members only portal of the NEPTUNE website (www.neptune-study.org). Data will be entered into the appropriate Velos CRF(s) as follows:

Visit		V2	V4	V6	V8	V10	V12	V13
Form 6A SF-36	Complete (x)	3	4					
	Date							
Form 6B PedsQL 2-4 (parent)	Complete (x)							
	Date							
Form 6C1 PedsQL 5-7 (child)	Complete (x)							
	Date							
Form 6C2 PedsQL 5-7 (parent)	Complete (x)							
	Date							
Form 6D1 PedsQL 8-12 (child)	Complete (x)							
	Date							
Form 6D2 PedsQL 8-12(parent)	Complete (x)							
	Date							
Form 6E1 PedsQL 13-17 (child)	Complete (x)							
	Date							
Form 6E2 PedsQL 13-17 (parent)	Complete (x)							
	Date							

CRFs are added to the participant's calendar via an "unscheduled event" (refer to your Velos Training Manual).

		Yes	No	Partially
Participant completed survey (select one):	5			

If *No* or *Partially* selected, please explain: 6

_____

_____

_____

7 Coordinator Signature: _____ Date: _____

8 Coordinator Name (Print): _____

Form 6A-E – Quality of Life Questionnaires v3 Feb-2012 Page 1 of 1

16.C.11.a. *Form 6A-E Quality of Life Questionnaires Worksheet Reference*

Header

1 Record participant's initials.

2 Record Patient ID.

Quality of Life Questionnaire

3 Under the appropriate Visit [#], select the appropriate QOL survey and indicate by marking an "X' and entering the date completed in the date box.

4 Example, if this was the 4-month follow-up visit [V4], this space would contain an "X" and the space below would indicate the date completed.

5 Indicate if the participant completed the survey ("Yes"), did not complete the survey ("No"), or only "Partially" completed the survey.

6 If "No" or "Partially" is selected, please provide an explanation.

7-8:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.12. Form 7 PROMIS Survey Worksheet

Participant Initials: __1____ See below for Visit Record

Patient ID: _____2_____

PROMIS Survey

Participant's User ID:	3
Password	4

Visit	Date Completed	Participant completed the PROMIS survey		If yes, Time to Complete:		If no, Indicate from key below*
		Yes	No	Hours	Minutes	
V2	5	6	7	8	9	10
V4						
V6						
V8						
V10						
V12						
V13						

* If participant did not complete the PROMIS Survey, please indicate 1 in the corresponding visit row:

A	Unable to access Assessment Center / technical problem
B	Does not read English
C	Less than 8 years of age
D	Participant declined
E	Other (explain below)

Any additional comments / problems:

11

_____

_____

_____

12 Coordinator Signature: _____ Date: _____

13 Coordinator Name (Print): _____

Form 7-PROMIS Survey v3 Feb-2012 Page 1 of 1

16.C.12.a. *Form 7 PROMIS Survey Worksheet Reference*

Header

1 Record participant's initials.

2 Record Patient ID.

3 Record your participant's PROMIS UserID for quick reference during study visits.

4 Record your participant's PROMIS Password for quick reference during study visits.

5 Record the date your participant completed the PROMIS assessment with the corresponding visit from the study visit calendar.

6 If the participant fully completed the PROMIS assessment, indicate by checking "Yes".

7 If the participant did not complete the PROMIS assessment, indicate by checking "No" and skip to question 10

8/9 Record the amount of time the participant required to complete the PROMIS assessment. Please record in hours and minutes.

10 If the participant did not complete the assessment, selecting from the key below, indicate why not according to the description.

11 Report any other comments or problems with the PROMIS assessment by indicating study visit "[V2]" and describing the concern.

12-13:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.13. Form 8 Baseline Biospecimens – *Adult* Worksheet

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

Baseline Biobank Specimens Collection – ADULT *(Adult=18 or older)*

4 Blood Draw Date:_____(mm/dd/yyyy)

PROCUREMENT				PROCESSING			Research Coordinator	
Blood Procured?			Y / N 5				Participant fasting?	Y / N / DK 8
Blood draw start time:			6 a.m. / p.m.	Blood processing start time		7 a.m. / p.m.	Hours *NPO: since last meal/non water beverage	9
Tube Top 10	Tube # 11	Type 12	Blood Procured? 13	# Tubes 14	Did foil remain intact? 15	# Cryovials 16	Please make notes of any aberrations below:	
Blue	1	Sodium Citrate	Y / N			Light blue caps (0-2)	17	
Orange	2	Foiled Serum	Y / N		Y / N	Orange cap DC (0 – 3)		
Tiger	3	SST (unfoiled)	Y / N			White Caps (0 – 3)		
Tiger	4	Foiled SST	Y / N		Y / N	White dot DC (0 – 3)		
Green	5	Sodium Heparin	Y / N		Y / N	Green cap DC (0 – 2)		
Purple	6 – 10	EDTA	Y / N			Red caps (0 – 17)		
Purple	11	EDTA - Chilled	Y / N		Chilled? Y / N	Purple Caps (0 – 3)		
Red	12	RNA PaxGene	Y / N		*Time at room temp* 18 minutes			
Black	13	DNA PaxGene	Y / N		*Time at room temp* 19 minutes			

20 DC = dark cryovials, all others clear

21 Prioritizations			
1 EDTA, 1 PAXGene required for every visit	Volume of EDTA is less essential than Volume for RNA tube (12)	DNA PAXGene only required ONE TIME over course of study	After obtaining the DNA tube, supplement blood draw with additional EDTA tubes not to exceed 8.5 mLs

22 ***Please return this worksheet to the proper Research Coordinator***

ADULT Form 8 Baseline Biospecimens Collection Worksheet v3.0

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

Baseline Biobank Specimens Collection – ADULT

24 hour urine

Procurement		
23 Urine Obtained?	Y	N
25 Date Collected		(mm/dd/yyyy)
26 Full 24H Collection	Y	N
28 Timed collection		minutes
		29 # Falcon Tubes (40 mL total)
		30 # 5 mL Aliquots (4.5 mL total)

Processing		
24 Total Volume		mL
Weight		grams
27 Tare	-	grams
28b Urine Weight*		grams
		(0 – 2)
		(0 – 5)

a

Urine weight = Weight – Tare

Spot/Random Clean Catch

Procurement		
31 Urine Procured?	Y / N	
32 Date Collected		(mm/dd/yyyy)
33 Participant Fasting?	Y / N / Don't Know	
34 Sample Collection	a.m. / p.m. / Don't Know	

Processing		
35 *Unprocessed:*		
# Whole urine aliquots		(0 – 4)
36 *Empty Samples:*		
37 # 15 mL tubes		(0 – 2)
38 # AS Aliquots		(0 – 4)
39 # AP E (Pellet) Aliquots		(0 – 2)
40 *PI (Protease Inhibitor) Samples:*		
41 # 15 mL tubes		(0 – 2)
42 # AQ Aliquots		(0 – 4)
43 # AP Q (pellet) Aliquots		(0 – 2)

Baseline – Nail Specimens

44 Obtained: Y/N Date mm/dd/yyy):_____45_____

Beginning with the big toe/thumb (digit 1) and ending with the pinky toe/finger (digit 5) indicate the sites from which specimens have been obtained (check all that apply):

Left	46 Foot	47 Hand	Not Available
Digit 1			
Digit 2			
Digit 3			
Digit 4			
Digit 5			

Right	Foot	Hand	Not Available
Digit 1			
Digit 2			
Digit 3			
Digit 4			
Digit 5			

Packing / Shipping – Outgoing:

(to NEPTUNE DACC)

Date Samples Packed (mm/dd/yyyy)	Time Samples Packed	Date Samples Shipped (mm/dd/yyyy)
48	49 a.m. p.m.	50

ADULT Form 8 Baseline Biospecimens Collection Worksheet v3.0

16.C.13.a. *Form 8 Baseline Biospecimens ADULT Worksheet Reference*

Please refer to Appendix M for the biospecimens processing manual of procedures. The following worksheet reference if for the adult baseline visit and can be used as a generalizable reference for all participant populations, including follow-up visits.

For sites using local research support staff (GCRC, Clinical Research Units, other lab staff), this updated biospecimens worksheet is organized to accommodate a sample *procurement* section (designated above by a red box outlining the relevant columns), as well as a *processing* section (designated above by the purple box outlining the relevant columns). Please be sure you pass on the updated worksheets and these Reference documents for your study staff, explaining the new form and contacting the NEPTUNE DACC for any necessary clarification.

Header

1 Record participant's initials.

2 Record the study visit date – even if it differs from the sample collection date(s).

3 Record Velos ID (e.g. 004021).

Blood Specimens

4 Please enter the date that the blood specimens were obtained in the format MM/DD/YYYY.

5 Record if blood was collected by circling "Y" for yes, or "N" for no.

6 Please enter the time the first blood specimen was obtained and indicate a.m. or p.m.

7 Please enter the time that blood specimen processing began and indicate a.m. or p.m.

8 Record if participant was fasting; check "Y" for yes, "N" for no, or "DK" for Don't Know.

9 Please record the number of hours since the participant has had food or a non-water beverage.

10 Noted here is the color of each vacutainer cap for reference.

11 Number assigned to the respective blood draw tube and in order which draw should occur.

12 Name of corresponding vacutainer used.

13 In relevance to the respective blood tube, circle "Y" for yes, or "N" for no if a sample was procured or not.

14 Please record the number of vacutainers collected for each type.

15 As applicable, indicate if the light-protective foil covering remained intact for the duration of the sample collection/processing.

16 Please record the number of filled cryovials obtained from processing the respective blood tube.

17 Please document any aberrations from the blood MOP in the space provided.

18 Please enter the time the RNA PAXgene tube spent at room temperature in minutes. The tube should sit for 2 hours at room temperature and then be placed in the freezer.

19 Please enter the time the DNA PAXgene tube spent at room temperature in minutes. The tube should sit for 2 hours at room temperature and then be placed in the freezer.

20 DC represents Dark Cryovials (used for samples from foiled tubes for light sensitive specimens).

21 Reference this chart for NEPTUNE blood draw prioritizations.

22 In the case of other laboratory personnel completing this worksheet, this worksheet must be returned to the RC upon processing completion for Velos data entry.

Urine Specimens

24-Hour Urine Samples

23 Please circle "Y" for yes, or "N" for no if a 24-hour urine specimen was obtained for the respective study visit.

24 Please enter the total volume of urine received in milliliters.

25 Please enter the date that the 24 hour urine specimen was obtained in the format MM/DD/YYYY

26 Please indicate whether a *full* 24 hour urine specimen was provided by circling "Y" (yes) or "N" (no).

27 Please record the Tare of the container used for 24 hour urine collection.

28a Please record the actual time of urine collection if <24 hour urine is collected for study sample.

28b Please enter the weight of the specimen (tare not included) in grams.

29 Please check the number of 50 mL Falcon tubes aliquoted for 24-hour urine specimens.

30 Please enter the number of 5 mL tubes aliquoted for 24-hour urine specimens.

Spot/Random Clean Catch Urine Samples

31 Please circle "Y" for yes, or "N" for no if a spot (random or fresh) urine specimen was obtained for the respective study visit.

32 Please enter the date that the random urine specimen was obtained in the format MM/DD/YYYY

33 Indicate if participant was fasting by circling "Y" for yes, or "N" for no. Please circle "Don't Know" if unknown.

34 Please circle "a.m." if the random urine was provided during the AM hours, and please circle "p.m." if the sample was provided during the PM hours. Please circle "Don't Know" if unknown.

Unprocessed Spot/Random Urine Sample

35 If > 60 mL of a spot/random clean catch urine is obtained, please aliquot 4 unprocessed samples into the whole urine ('SU') aliquots.

Supernatant Samples (Empty): From the empty 15 mL centrifuge tubes, indicate:

36 'Line items 37-39 refer to the samples processed from the "Empty" 15 mL centrifuge tubes.

37 Number of "EMPTY" 15 mL centrifuge tubes filled to the 12 mL mark (0-2).

38 Number of spun supernatant Sodium Azide ('AS') aliquots (0-4).

39 Number of spun pellet aliquots 'AP E' (0-2).

Supernatant Samples from Protease Inhibitor (PI): From the PI 15 mL centrifuge tubes, indicate:

40 Line items 41-43 refer to the samples processed from the "PI" 15 mL centrifuge tubes.

41 Number of "PI" 15 mL centrifuge tubes filled to the 12 mL mark (0-2).

42 Number of spun supernatant 'AQ' aliquots (0-4).

43 Number of spun pellet aliquots 'AP Q' (0-2).

Nail Specimens

44 Please circle "Y" for yes, or "N" for no to indicate if nail specimens were obtained for the respective study visit.

45 Please enter the date the nail specimens were obtained in the format MM/DD/YYYY.

46 Please indicate, by checking, from which digit on which hand or foot nail specimens have been obtained. Check all that apply. Under normal circumstances, you should obtain 10 nail specimens (e.g. 10 from all ten fingers or 10 from all ten toes).

47 Please indicate, by checking, from which digit on which hand or foot nail specimens have been obtained. Check all that apply. Under normal circumstances, you should obtain 10 nail specimens (e.g. 10 from all ten fingers or 10 from all ten toes).

Packing / Shipping (outgoing: to NEPTUNE)

48 Please document on each participant kit specimen form the date samples were packed in the format MM/DD/YYYY.

49 Indicate the time each participant kit was packed and circle a.m. or p.m.

50 Record the date the samples were picked up by your local courier in the format MM/DD/YYYY.

16.C.14. Form 8 Baseline Biospecimens *Pediatrics* Worksheet

Participant Initials:____ 1____ Visit Date:_____ 2_____

Patient ID:_____ 3_____

Baseline Biobank Specimens Collection – PEDS ≥ 52 lbs.

4 Blood Draw Date:_____(mm/dd/yyyy)

PROCUREMENT				PROCESSING			Research Coordinator	
Blood Procured?			5 Y / N				Participant fasting?	Y / N / DK 8
Blood draw start time:			6 a.m. / p.m.	Blood processing start time:		7 a.m. / p.m.	Hours *NPO: since last meal/non water beverage	9
Tube Top 10	Tube # 11	Type 12	Blood Procured? 13	# Tubes 14	Did foil remain intact? 15	# Cryovials 16	Please make notes of any aberrations below:	
Blue	1	Sodium Citrate	Y / N			Light blue caps (0-2)	17	
Orange	2	Foiled Serum	Y / N		Y / N	Orange cap DC (0 – 3)		
Tiger	3	SST (unfoiled)	Y / N			White Caps (0 – 3)		
Tiger	4	Foiled SST	Y / N		Y / N	White dot DC (0 – 3)		
Green	5	Sodium Heparin	Y / N		Y / N	Green cap DC (0 – 2)		
Purple	6 – 9, 15	EDTA	Y / N			Red caps (0 – 14)		
Purple	14	EDTA - Chilled	Y / N		Chilled? Y / N	Purple Caps (0 – 2)		
Red	12	RNA PaxGene	Y / N		*Time at room temp* 18 minutes			
Black	13	DNA PaxGene	Y / N		*Time at room temp* 19 minutes			

20 DC = dark cryovials, all others clear

21 Prioritizations				
1 EDTA, 1 PAXGene required for every visit	Volume of EDTA is less essential than Volume for RNA tube (12)	DNA PAXGene only required ONE TIME over course of study	Visits using tube 15: 5 mLs is IRB approved volume	Pediatric Weight Key: < 21 lbs.= <9.5 kg 21-51 lbs. = 9.5 - 23.1 kg ≥ 52 lbs.= ≥ 23.6 kg

22 ***Please return this worksheet to the proper Research Coordinator***

Participant Initials:____ 1____ Visit Date:_____ 2_____

Patient ID:_____ 3_____

Baseline Biobank Specimens Collection – PEDS ≥ 52 lbs.

24 hour urine

Procurement		
23 Urine Procured?	Y	N
25 Date Collected		(mm/dd/yyyy)
26 Full 24H Collection	Y	N
28 Timed collection		minutes
		29 # Falcon Tube (40 mL total)
		30 # 5 mL Aliquot (4.5 mL total)

**Urine weight = Weight - Tare*

Processing		
24 Total Volume		mL
Weight		grams
27 Tare	-	grams
28 Urine Weight*		grams
(40 mL total)		(0 – 2)
(4.5 mL total)		(0 – 5)

Spot/Random Clean Catch

Procurement		
31 Urine Procured?	Y / N	
32 Date Collected		(mm/dd/yyyy)
33 Participant Fasting?	Y / N / Don't Know	
34 Sample Collection	a.m. / p.m. / Don't Know	

Processing		
35 *Unprocessed:*		
# SU (Whole urine) aliquots		(0 – 4)
36 *Empty Samples:*		
37 # 15 mL tubes		(0 – 2)
38 # AS Aliquots		(0 – 4)
39 # AP E (Pellet) Aliquots		(0 – 2)
40 *PI (Protease Inhibitor) Samples:*		
41 # 15 mL tubes		(0 – 2)
42 # AQ Aliquots		(0 – 4)
43 # AP Q (pellet) Aliquots		(0 – 2)

Baseline – Nail Specimens

44 Obtained: Y/N **Date** mm/dd/yyyy):_____45_____

Beginning with the big toe/thumb (digit 1) and ending with the pinky toe/finger (digit 5) indicate the sites from w
specimens have been obtained (check all that apply):

Left	46 Foot	47 Hand	Not Available
Digit 1			
Digit 2			
Digit 3			
Digit 4			
Digit 5			

Right	Foot	Hand	Not Available
Digit 1			
Digit 2			
Digit 3			
Digit 4			
Digit 5			

Packing / Shipping – Outgoing:

(to NEPTUNE DACC)

Date Samples Packed (mm/dd/yyyy)	Time Samples Packed	Date Samples Shipped (mm/dd/yyyy)
48	49 a.m. p.m.	50

16.C.14.a. *Form 8 Baseline Biospecimens Pediatrics Worksheet Reference*

Please refer to Appendix M for the biospecimens processing manual of procedures. The following worksheet reference if for the pediatric **≥ 52 lbs** baseline visit and can be used as a generalizable reference for all participant populations, including follow-up visits. Pediatric worksheets and Velos CRF's should be chosen carefully and according to the participant's study visit weight. If the corresponding kit is not available, use the kit on-hand, documenting in your worksheet the reason for the incorrect weight blood draw.

For sites using local research support staff (GCRC, Clinical Research Units, other lab staff), this updated biospecimens worksheet is organized to accommodate a sample *procurement* section (designated above by a red box outlining the relevant columns), as well as a *processing* section (designated above by the purple box outlining the relevant columns). Please be sure you pass on the updated worksheets and these Reference documents for your study staff, explaining the new form and contacting the NEPTUNE DACC for any necessary clarification.

Header

1 Record participant's initials.

2 Record the study visit date – even if it differs from the sample collection date(s).

3 Record Velos ID (e.g. 004021).

Blood Specimens

4 Please enter the date that the blood specimens were obtained in the format MM/DD/YYYY.

5 Record if blood was collected by circling "Y" for yes, or "N" for no.

6 Please enter the time the first blood specimen was obtained and indicate a.m. or p.m.

7 Please enter the time that blood specimen processing began and indicate a.m. or p.m.

8 Record if participant was fasting; check "Y" for yes, "N" for no, or "DK" for Don't Know.

9 Please record the number of hours since the participant has had food or a non-water beverage.

10 Noted here is the color of each vacutainer cap for reference.

11 Number assigned to the respective blood draw tube and in order which draw should occur.

12 Name of corresponding vacutainer used.

13 In relevance to the respective blood tube, circle "Y" for yes, or "N" for no if a sample was procured or not.

14 Please record the number of vacutainers collected for each type.

15 As applicable, indicate if the light-protective foil covering remained intact for the duration of the sample collection/processing.

16 Please record the number of filled cryovials obtained from processing the respective blood tube.

17 Please document any aberrations from the blood MOP in the space provided.

18 Please enter the time the RNA PAXgene tube spent at room temperature in minutes. The tube should sit for 2 hours at room temperature and then be placed in the freezer.

19 Please enter the time the DNA PAXgene tube spent at room temperature in minutes. The tube

should sit for 2 hours at room temperature and then be placed in the freezer.

20 DC represents Dark Cryovials (used for samples from foiled tubes for light sensitive specimens).

21 Reference this chart for NEPTUNE blood draw prioritizations.

22 In the case of other laboratory personnel completing this worksheet, this worksheet must be returned to the RC upon processing completion for Velos data entry.

Urine Specimens

24-Hour Urine Samples

23 Please circle "Y" for yes, or "N" for no if a 24-hour urine specimen was obtained for the respective study visit.

24 Please enter the total volume of urine received in milliliters.

25 Please enter the date that the 24 hour urine specimen was obtained in the format MM/DD/YYYY

26 Please indicate whether a *full* 24 hour urine specimen was provided by circling "Y" (yes) or "N" (no).

27 Please record the Tare of the container used for 24 hour urine collection.

28a Please record the actual time of urine collection if <24 hour urine is collected for study sample.

28b Please enter the weight of the specimen (tare not included) in grams.

29 Please check the number of 50 mL Falcon tubes aliquoted for 24-hour urine specimens.

30 Please enter the number of 5 mL tubes aliquoted for 24-hour urine specimens.

Spot/Random Clean Catch Urine Samples

31 Please circle "Y" for yes, or "N" for no if a spot (random or fresh) urine specimen was obtained for the respective study visit.

32 Please enter the date that the random urine specimen was obtained in the format MM/DD/YYYY

33 Indicate if participant was fasting by circling "Y" for yes, or "N" for no. Please circle "Don't Know" if unknown.

34 Please circle "a.m." if the random urine was provided during the AM hours, and please circle "p.m." if the sample was provided during the PM hours. Please circle "Don't Know" if unknown.

Unprocessed Spot/Random Urine Sample

35 If > 60 mL of a spot/random clean catch urine is obtained, please aliquot 4 unprocessed samples into the whole urine ('SU') aliquots.

Supernatant Samples (Empty): From the empty 15 mL centrifuge tubes, indicate:

36 'Line items 37-39 refer to the samples processed from the "Empty" 15 mL centrifuge tubes.

37 Number of "EMPTY" 15 mL centrifuge tubes filled to the 12 mL mark (0-2).

38 Number of spun supernatant Sodium Azide ('AS') aliquots (0-4).

39 Number of spun pellet aliquots 'AP E' (0-2).

Supernatant Samples from Protease Inhibitor (PI): From the PI 15 mL centrifuge tubes, indicate:

40 Line items 41-43 refer to the samples processed from the "PI" 15 mL centrifuge tubes.

41 Number of "PI" 15 mL centrifuge tubes filled to the 12 mL mark (0-2).

42 Number of spun supernatant 'AQ' aliquots (0-4).

43 Number of spun pellet aliquots 'AP Q' (0-2).

Nail Specimens

44 Please circle "Y" for yes, or "N" for no to indicate if nail specimens were obtained for the respective study visit.

45 Please enter the date the nail specimens were obtained in the format MM/DD/YYYY.

46 Please indicate, by checking, from which digit on which hand or foot nail specimens have been obtained. Check all that apply. Under normal circumstances, you should obtain 10 nail specimens (e.g. 10 from all ten fingers or 10 from all ten toes).

47 Please indicate, by checking, from which digit on which hand or foot nail specimens have been obtained. Check all that apply. Under normal circumstances, you should obtain 10 nail specimens (e.g. 10 from all ten fingers or 10 from all ten toes).

Packing / Shipping (outgoing: to NEPTUNE)

48 Please document on each participant kit specimen form the date samples were packed in the format MM/DD/YYYY.

49 Indicate the time each participant kit was packed and circle a.m. or p.m.

50 Record the date the samples were picked up by your local courier in the format MM/DD/YYYY.

16.C.15. Form 9 Adverse Event Reporting Worksheet

***Please see the reference below for a complete description of each numbered question.**

ADVERSE EVENT REPORTING WORKSHEET
[FORM 9]

3 **Adverse Event Occurrence Date:**_____/_____/_____

4 **Adverse Event Report Date:**_____/_____/_____

5 **Adverse Event Name (Use CTCAE v3.0):**_____

6 **Was this a Serious Adverse Event (IF SERIOUS, IMMEDIATELY ENTER INTO VELOS AND REPORT TO YOUR LOCAL IRB):**

□ Yes □ No

7 **Adverse Event Grade:**

□ Grade 1 (Mild) □ Grade 2 (Moderate) □ Grade 5 (Death)

□ Grade 3 (Severe) □ Grade 4 (Life Threatening/Disabling)

8 **Description of Adverse Event (Include Location of Treatment and Event Outcome):**

_____

_____

_____

_____

9 **Was Adverse Event Expected (Was it listed as a known or expected risk in the Consent Form)?**

□ Yes □ No

10 **Relationship of the Adverse Event to Research Procedures: (*Relationship must be given by the treating physician)**

□ Definitely Not Related □ Probably Not Related □ Possibly Related □ Probably Related
□ Definitely Related

11 **Was the Adverse Event associated with any of the following? (Check all that apply)**

□ Development of a congenital anomaly or birth defect

□ Development of a permanent, serious, disabling or incapacitating condition

□ Death: _____/_____/_____(date of death)

□ Hospitalization or Prolonged Hospitalization

□ Life Threatening

12 **Adverse Event Resolution Date:**_____/_____/_____

13 **Additional Comments:**_____

16.C.15.a. *Form 9 Adverse Event Reporting Worksheet Reference*

Header

1 Record participant's initials.

2 Record participant ID.

Adverse Event Information

3 Enter the date that the Adverse Event occurred or began.

4 Enter the date that the Adverse Event Worksheet was completed

5 Refer to the CTCAE v3.0 to provide the proper name for the Adverse Event and record the name here. In the VELOS AE Case Report Form you will select an Adverse Event from a list of CTCAE terms. After you have chosen the correct CTCAE Term the "Event Category", "Supra-term", "Modifier", "Severity", and "Event Details" will populate.

6 By the definition of a Serious Adverse Event (An event that results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; creates persistent or significant disability/incapacity, or a congenital anomaly/birth defect) is the event considered serious.

7 Refer to the CTCAE v3.0 to provide the proper grade for the Adverse Event.

8 Please describe the event in detail. Include the location of treatment, types of treatment and event outcome.

9 Please refer to the consent form to see if the adverse event has been listed as a potential risk. If the adverse event is listed as a risk, please check "Yes" and if it was not listed, please check "No."

10 Please consult the treating physician for the attribution (whether or not the event was related to research procedures) of the adverse event.

11 Please check all that apply. If the event was associated with death, please enter the date of death.

12 Please enter the date that the Adverse Event resolved if it is available. If the resolution date is not yet known, leave this section blank and enter in the date when the event has resolved.

13 Please enter any additional comments about the Adverse Event here.

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.16. Form 10 Baseline Labs Worksheet

*Please see the reference below for a complete description of each numbered question.

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

BASELINE LABS

4 If a lab result is not available, leave the date field (1st column) blank, enter "NA" in the value field (2nd column) and leave the units field (3rd column) as is.

UA (Urinalysis, macroscopic)

5 **Results Determined By:** Local Lab MD

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
Color	/ /	6	
Appearance	/ /	7	
Specific Gravity	/ /	8	
pH	/ /	9	
Leuk Est	/ /	10	
Nitrite	/ /	11	
Protein	/ /	12	
Glucose	/ /	13	
Ketones	/ /	14	
Urobilin	/ /	15	
Bilirubin	/ /	16	
Blood	/ /	17	

RANDOM (SPOT) URINE

Either a Protein or Creatinine result is REQUIRED

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
Protein	/ /	18	
Creatinine	/ /	19	
Protein / Creat Ratio	/ /	20	
Albumin	/ /	21	

24-HOUR URINE or TIMED URINE COLLECTION

Form 10 Baseline Labs Worksheet v3 FEB-2012 Page 1 of 6

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

18 ▯ **24-Hour Urine** ▯ **Timed Urine –**

19 **If Timed Urine, total collection time (hh:mm): _____**

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
Urine Total Creatinine	/ /	20	
Urine Total Volume	/ /	21	
Creatinine Clearance	/ /	22	
Urine Total Protein	/ /	23	
Urine Total Albumin	/ /	24	

CBC

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
WBC	/ /	25	
Hemoglobin	/ /		
Hematocrit	/ /		
Platelets	/ /		
MCV	/ /		
MCH	/ /		
MCHC	/ /		

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

COMPREHENSIVE METABOLIC PANEL

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
Sodium	/ /	26	
Potassium	/ /		
Chloride	/ /		
CO2	/ /		
Urea Nitrogen	/ /		
Creatinine	/ /		
Glucose	/ /		
Calcium	/ /		
Protein	/ /		
Albumin	/ /		
AST	/ /		
ALT	/ /		
Alkaline Phosphatase	/ /		
Total Bilirubin	/ /		

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
A1C	/ /		
Magnesium	/ /		
Phosphorus	/ /		

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

OTHER

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
CRP 27	/ /		

Test Name	Test Date (MM/DD/YYYY)	Result Value
ANCA 28	_____/_____/_____	☐ Not Available ☐ Negative ☐ Positive – Titer: _____ ☐ Other – Specify: _____
ENA 29	_____/_____/_____	☐ Not Available ☐ Negative ☐ Positive – Check all that apply: ☐ SS-A (Ro) ☐ SS-B (La) ☐ Smith ☐ SmRNP ☐ RNP ☐ Jo-1 ☐ Scleroderma (Scl-70) ☐ Centromere B ☐ Chromatin ☐ ds-DNA ☐ Ribosomal P ☐ Other – Specify: _____
ANA 30	_____/_____/_____	☐ Not Available ☐ Negative ☐ Positive – Titer: _____ ☐ Other – Specify: _____

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
Anti dsDNA 31	/ /		

Test Name	Test Date (MM/DD/YYYY)	Result Value
Cryoglobulins 32	_____/_____/_____	☐ Not Available ☐ Negative ☐ Positive ☐ Other – Specify:

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

Test Name	Test Date (MM/DD/YYYY)	Result Value (NA if Not Available)	Result Units
C3 33	/ /		
C4 34	/ /		

Test Name	Test Date (MM/DD/YYYY)	Result Value
Anti GBM 35	_____/_____/_____	◻ Not Available ◻ Negative ◻ Positive – Titer: _____ ◻ Other – Specify: _____
Anti SLT 36	_____/_____/_____	◻ Not Available ◻ Negative ◻ Positive ◻ Other – Specify:

INFECTION

Test Name	Test Date (MM/DD/YYYY)	Result Value
Hepatitis B 37	_____/_____/_____	◻ Not Available ◻ Negative ◻ Positive Specify Test: _____ ◻ Indeterminate Specify Test: _____
Hepatitis C 38	_____/_____/_____	◻ Not Available ◻ Negative ◻ Positive Specify Test: _____ ◻ Indeterminate Specify Test: _____
EBV 39	_____/_____/_____	◻ Not Available ◻ Negative ◻ Positive Specify Test: _____ ◻ Indeterminate Specify Test:

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

Test Name	Test Date (MM/DD/YYYY)	Result Value
CMV 40	____/____/____	☐ Not Available ☐ Negative ☐ Positive Specify Test: _____ ☐ Indeterminate Specify Test: _____
HIV 41	____/____/____	☐ Not Available ☐ Negative ☐ Positive Specify Test: _____ ☐ Indeterminate Specify Test: _____
Hantavirus 42	____/____/____	☐ Not Available ☐ Negative ☐ Positive Specify Test: _____ ☐ Indeterminate Specify Test: _____
Parvovirus 43	____/____/____	☐ Not Available ☐ Negative ☐ Positive Specify Test: _____ ☐ Indeterminate Specify Test:

44 Coordinator Signature: _____ Date: _____

45 Coordinator Name (Print): _____

Form 10 Baseline Labs Worksheet v3 FEB-2012 Page 6 of 6

16.C.16.a. *Form 10 Baseline Labs Worksheet Reference*

***The information recorded on this worksheet may differ based on the ordering physician. Please use lab results that have occurred within 30 days prior to the visit. Also, if there are multiple results, please use the most recent data associated with this visit (e.g. If you have data from 28 days prior and data from two weeks prior, please enter the data from two weeks prior).**

EFFECTIVE 12/01/2012: Please document ALL lab values and dates corresponding to the nearest study visit. Lab data should not be "double entered" for more than one study visit, but determined for which visit is most proximate and recorded appropriately.

Header

1 Record participant's initials.

2 Record the study visit date.

3 Record Patient ID.

4 **If a lab result is not available, leave the date field blank (column "Test Date"), enter "NA" in the value field ("Result Value"), and do not mark anything in the "Results Units" in the worksheet.**

Urinanalysis, macroscopic

5 Record if sample was evaluated by clinician at clinic visit or reviewed from the medical chart for a sample processed by the site's clinical labs.

6 Record the color result (e.g. Normal)

7 Record the appearance (e.g. Normal or Cloudy).

8 Record the specific gravity.

9 Record the urine pH.

10 Record the leukocyte esterase result (e.g. Negative or number result with units)

11 Record the urine nitrite result (e.g. Negative)

12 Record the urine protein result (e.g. Negative or 30mg/dl)

13 Record the urine glucose result (e.g. Negative or 300mg/dl).

14 Record the urine ketone result.

15 Record the urine urobilin result (e.g. Normal).

16 Record the urine bilirubin result.

17 Record the urine blood result.

Random Spot Urine (Fresh urine)

18 Record the urine protein result and units.

19 Record the urine creatinine result and units.

20 Record the urine protein/creatinine ratio.

21 Record the urine abumin result and units.

24 Hour Urine

18 Indicate if the urine collection was a 24-hour sample or a timed urine.

19 If sample is a timed urine, indicate the total collection time in hh:mm format.

20 Record the urine total creatinine result and units.

21 Record the urine total volume result and units.

22 Record the creatinine clearance result and units.

23 Record the urine total protein result and units.

24 Record the urine total albumin result and units.

CBC

25 Complete the table, entering the date in the left open column, measurement in the center column and units in the right open column. If a measurement was not done (e.g. MCV was not done) please enter NA in the 2nd column.

Comprehensive Metabolic Panel

26 Complete the table, entering the date in the left open column, measurement in the center column and units in the right open column. If a measurement was not done (e.g. magnesium was not done) please enter NA in the 2nd column.

Other

27 If CRP (c-reactive protein) was not done please enter NA in the results column. If it was obtained, please record the date, result and units.

28 If ANCA (anti-neutrophil cytoplasmic antibody) was not done please enter NA in the results column. If it was obtained, please record the date and check positive, negative, or other. If other, please explain.

If ANCA was positive, please record the titer and units.

29 If ENA (extractable nuclear antigens) was not done please check the "Not Done" box. If it was obtained, please record the date and check positive, negative, or other. If other, please explain.

If ENA was positive, please check the box(s) that corresponds to the elevated antigen(s).

30 If ANA (anti-nuclear antibody) was not done please check the "Not Done" box. If it was obtained, please record the date and check positive, negative, or other. If other, please explain.

If ANA was positive, please record the titer and units.

31 If Anti dsDNA (anti-double stranded DNA) was not done please check the "Not Done" box. If it was obtained, please record the date, result and units.

32 If Cryoglobulins were not done please check the "Not Done" box. If they were obtained, please record the date and check positive, negative, or other. If other, please explain.

33 If C3 (complement component 3) was not done please check the "Not Done" box. If it was obtained, please record the date, result and units.

34 If C4 (complement component 4) was not done please check the "Not Done" box. If it was obtained, please record the date, result and units.

35 If Anti GBM (anti-glomerular basement membrane antibody) was not done please check the "Not Done" box. If it was obtained, please record the date and check positive, negative, or other. If other, please explain.

If Anti-GBM was positive, please record the titer and units.

36 If Anti SLT(anti-streptolysin titer) was not done please check the “Not Done” box. If it was obtained, please record the date and check positive, negative, or other. If other, please explain.

Infection

37 If Hepatitis B test was not done please check the “Not Done” box. If it was obtained, please record the date and check positive, negative, or indeterminate. If positive or indeterminate, please record the test type (i.e. PCR or ELISA).

38 If Hepatitis C test was not done please check the “Not Done” box. If it was obtained, please record the date and check positive, negative, or indeterminate. If positive or indeterminate, please record the test type (i.e. PCR or ELISA).

39 If EBV (Eptstein-Barr Virus) test was not done please check the “Not Done” box. If it was obtained, please record the date and check positive, negative, or indeterminate. If positive or indeterminate, please record the test type (i.e. PCR or ELISA).

40 If CMV (Cytomegalovirus) test was not done please check the “Not Done” box. If it was obtained, please record the date and check positive, negative, or indeterminate. If positive or indeterminate, please record the test type (i.e. PCR or ELISA).

41 If HIV test was not done please check the “Not Done” box. If it was obtained, please record the date and check positive, negative, or indeterminate. If positive or indeterminate, please record the test type (i.e. PCR or ELISA).

42 If Hantavirus test was not done please check the “Not Done” box. If it was obtained, please record the date and check positive, negative, or indeterminate. If positive or indeterminate, please record the test type (i.e. PCR or ELISA).

43 If Parvovirus test was not done please check the “Not Done” box. If it was obtained, please record the date and check positive, negative, or indeterminate. If positive or indeterminate, please record the test type (i.e. PCR or ELISA).

44-44:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.17. Form 11A Kidney Specimens Worksheet

***Please see the reference below for a complete description of each numbered question.**

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

KIDNEY SPECIMENS

PART I. (Complete immediately following biopsy)

Kidney Tissue

Biopsy Date:	4				
Kidney Biopsy Specimen obtained for study:		5	Yes	6	No
Number of Passes (usually from procedure note)		7	Number	8	Unknown

Set Form Status to "Completed" at the bottom left.

PART II. (Complete immediately upon receipt of local histology report)

Date Part II completed:_____9_____

Even if a kidney biopsy specimen is not obtained for the study, the local histology report is still required.

10 Please attach a printed copy of the de-identified (including all patient identifiers – name, age/DOB, gender, race – and physician information) local histology report. This information should be copied and pasted (with PHI removed, including Patient Name, age/DOB, gender, race and Caregiver information) into the appropriate Velos CRF fields (Form 11A).

Set Form Status to "Completed" at the bottom left.

Event status should not be changed to "Done" unless all Parts (I, II and III) are complete.

11 Coordinator Signature:_____ Date:_____

12 Coordinator Name (Print):_____

Form 11A Kidney Specimens v3.1 Feb-2012 Page 1 of 1

16.C.17.a. *Form 11A Kidney Specimens Worksheet Reference*

***The information recorded on this worksheet must be entered into Velos promptly.**

Header

1 Record participant's initials.

2 Record the study visit date.

3 Record Patient ID.

Part I. Kidney Specimen

4 Record the date of the participant's clinically indicated renal biopsy

5 Record if a renal core was obtained and released for study purpose.

6 Record if a renal core was not available for study purpose and report to the NEPTUNE DACC.

7 Document the number of passes required for the biopsy procedure. Many sites' hospitals will record this information in a "procedure note".

8 If you are unable to locate the number of passes required during the biopsy procedure, please check the "Unknown" box and document in the Velos CRF form.

Part II. Pathology Report

9 Document the date the kidney specimen final report was completed.

10 Attach a printed copy of the de-identified (including all patient identifiers – name, age/DOB, gender, race – and physician information) local histology report to this form and keep in the participant's shadow/research chart. This information should be copied and pasted (with PHI removed, including Patient Name, age/DOB, gender, race and Caregiver information) into the appropriate Velos CRF fields (Form 11A).

11-12:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.18. Form 11A-Slides Case Report Form (CRF)

There is not a separate worksheet for Form 11A-Slides. Prior to shipping slides to the NIDDK, completing this CRF will enable the NIDDK to be prepared for your shipment and create the necessary barcodes for scanning and uploading. Slides must ***not*** be shipped without completion of the form.

***Please see the reference below for a complete description of each numbered question.**

Form Name: 11A-Slides - Kidney Specimens Slides

Nephrotic Syndrome Study Network (NEPTUNE)

Kidney Specimens Slides
(Form 11A-Slides)

1 **Visit Date (V3):*** 02/22/2012

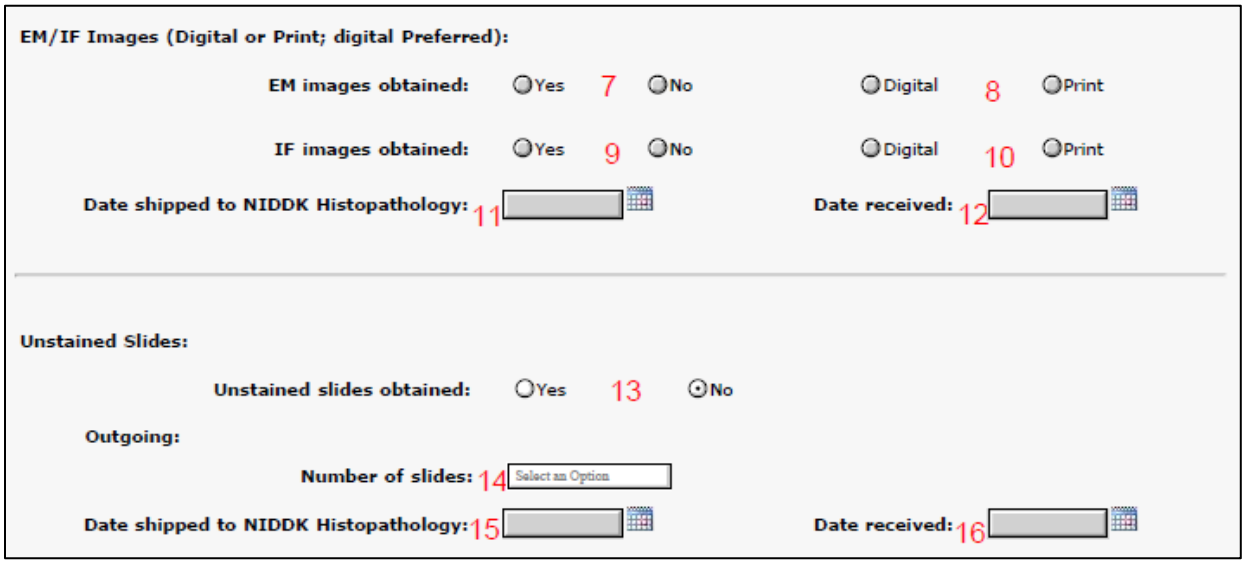
Local Pathology Slides

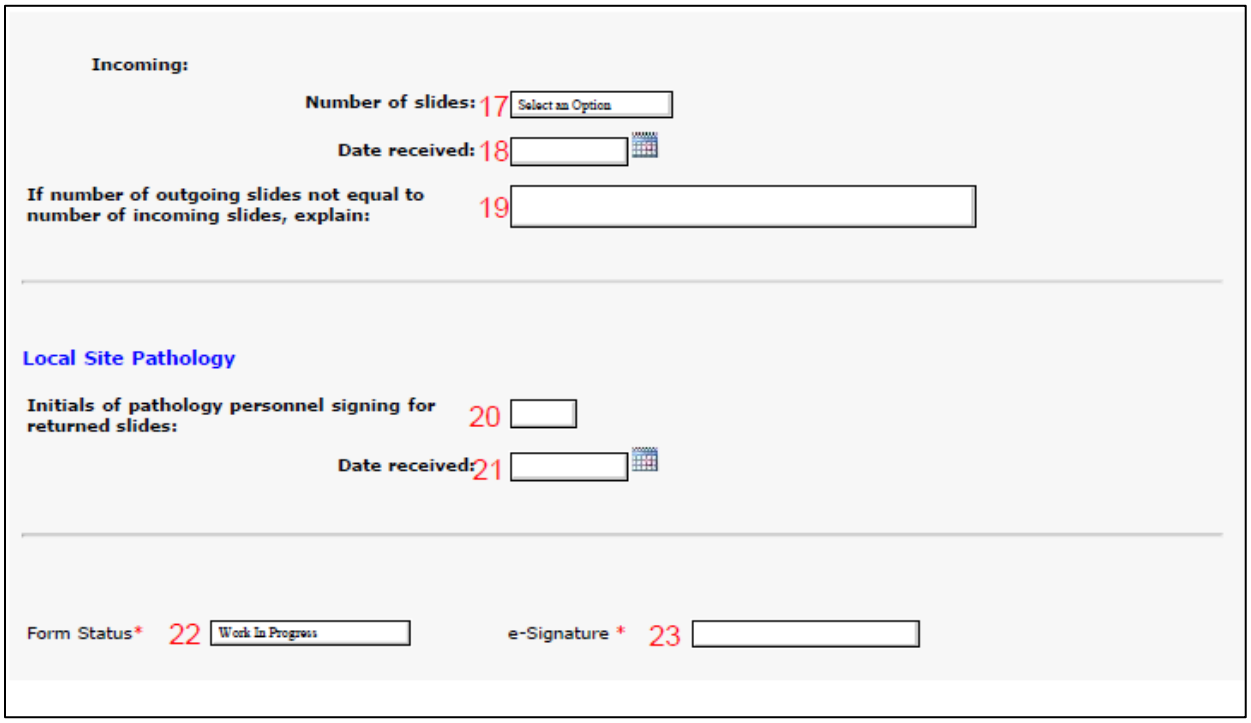
Stained Slides:

Stained slides obtained: 2 ○Yes 3 ○No

Outgoing:

4	☐ Slide 1	Level Number:	5	Stain: 6	Select an Option
	☐ Slide 2	Level Number:		Stain:	Select an Option
	☐ Slide 3	Level Number:		Stain:	Select an Option
	☐ Slide 4	Level Number:		Stain:	Select an Option
	☐ Slide 5	Level Number:		Stain:	Select an Option
	☐ Slide 6	Level Number:		Stain:	Select an Option
	☐ Slide 7	Level Number:		Stain:	Select an Option
	☐ Slide 8	Level Number:		Stain:	Select an Option
	☐ Slide 9	Level Number:		Stain:	Select an Option
	☐ Slide 10	Level Number:		Stain:	Select an Option
	☐ Slide 11	Level Number:		Stain:	Select an Option
	☐ Slide 12	Level Number:		Stain:	Select an Option
	☐ Slide 13	Level Number:		Stain:	Select an Option
	☐ Slide 14	Level Number:		Stain:	Select an Option
	☐ Slide 15	Level Number:		Stain:	Select an Option


EM/IF Images (Digital or Print; digital Preferred):
EM images obtained: Yes 7 No Digital 8 Print
IF images obtained: Yes 9 No Digital 10 Print
Date shipped to NIDDK Histopathology: 11
Date received: 12
Unstained Slides:
Unstained slides obtained: Yes 13 No
Outgoing:
Number of slides: 14 Select an Option
Date shipped to NIDDK Histopathology: 15
Date received: 16


Incoming:
Number of slides: 17 Select an Option
Date received: 18
If number of outgoing slides not equal to number of incoming slides, explain: 19
Local Site Pathology
Initials of pathology personnel signing for returned slides: 20
Date received: 21
Form Status* 22 Work In Progress
e-Signature * 23

16.C.18.a. *Form 11A Kidney Specimens Slides Worksheet Reference*

***The information recorded on this worksheet must be entered into Velos promptly.**

Header

1 Document the date of initiating this form.

Part I. Local Pathology Slides - Outgoing

2 Document if stained slides were obtained for digitization at the NIDDK Histopathological Archive. Independent of study biopsy core tissue. (If renal tissue was not obtained for the research study, please continue to request slides).

3 If stained slides are not available for NIDDK Biorepository scanning, please contact the NEPTUNE DACC.

4 For each slide obtained check a box indicating number.

5 For each slide obtained, enter the level number indicated on the de-identifying label.

6 If known, indicate the slide stain in the corresponding row.

EM/IF Images - Outgoing

7 Indicate if electron microscopy (EM) images were obtained.

8 Indicate if the EM images are digital or print.

9 Indicate if immunofluorescence (IF) images were obtained.

10 Indicate if IF images are digital or print.

11 Record the date all stained slides and images will be shipped to the NIDDK Histopathology Archive.

12 Record the date stained slides and images are received by the NIDDK Histopathology Archive from the Slide Requisition form.

Unstained Slides – Outgoing

13 Indicate if unstained slides were obtained for the NEPTUNE study.

14 Record how many unstained slides are being sent to the NIDDK Histopathology Archive.

15 Record the date unstained slides will be shipped to the NIDDK Histopathology Archive.

16 Record the date unstained slides are received by the NIDDK Histopathology Archive from the Slide Requisition form.

Incoming

17 Record the number of slides returned to the local site.

18 Record the date stained slides are returned from the NIDDK Histopathology Archive to the local site.

19 If the number of outgoing, stained slides is not equal to what was returned, document here and contact the NEPTUNE DACC.

20 Document the local site's pathology personnel initials receiving the stained slides.

21 Record the date stained slides are returned to the local site pathology department.

22 Upon data entry into 20 and 21 above, indicate the form as "Done".

23 Enter your Velos e-signature and indicate the event as “Done”.

16.C.19. Form 11B Slide Shipment Manifest –SITE TO NIDDK

*Please see the reference below for a complete description of each numbered item.

SLIDE SHIPMENT MANIFEST
SITE TO NIDDK

A. OUTGOING: Shaded sections to be completed by the Site Research Coordinator (Shipper). The original form will be maintained in the participant research chart locally. A completed copy of Form 11B will serve as the shipping manifest and should be sent to the NIDDK along with:

1. Requested slides
2. De-identified copy of the local histology report
3. EM prints or disk
4. Form 11C – Stained Slide Return Manifest (reverse)

Mailing address for pathology materials:

Ms. Lisa Swearinger
Kidney Disease Section
10 Center Dr, Room 3N116 NIH
Bethesda, MD 20892-1268

Tel: 301-496-3092
lisas@intra.niddk.nih.gov

Stained Slides		
# Slides Shipped	Date Received	Comments
1		
Unstained Slides		
# Slides Shipped	Date Received	Comments
2		
EM Images & Pathology Report		
Disk Contents	Report	Disk Received / Date
3 □ De-identified Images □ De-identified Pathology Report	4 □ Indicate here if hard-copy path report enclosed Request for print return? □ Yes □ No	Date Received _____ Comments: _____

Shipper 5

Coordinator Name: _____ Address: _____
Phone: _____ Address: _____
Fax: _____ City: _____
Shipper Signature: _____ State/Zip: _____

B. RECEIVED: This section is to be completed by the receiver. Upon receipt of pathology packet, completed form should be faxed to research coordinator named above.

Receiver Name (Printed): _____ Date _____
Receiver Signature _____

ATTENTION:

6

FAX:

(Shipper's name and fax here)

Form 11B Slide Shipment Manifest V3.0 FEB-2012

16.C.19.a. *Form 11B/C Slide Shipment Manifest Reference – Part I*

Form 11B/C is a four-part process. Please review all instructions below and document as necessary in Velos.

Form 11B: The local site research coordinator should complete the shaded sections for items shipped, as described below. Send the requested materials (stained slides, de-identified copy of the local histology report, EM prints or digital images burned to disk, and Form C to the NIDDK Histopathological Archive via "Ground" service through the UPS shipping portal (see Appendix N).

Maintain the original document in the local research/shadow chart and include a copy of Form 11B with the shipment.

Part I. Manifest Form 11B Responsibilities – Research Coordinator:

1 Please indicate the total number of stained slides being shipped.

2 Please indicate the total number of unstained* ("blank") slides being shipped.

3 Please indicate what is documented on the compact disk.

4 Please indicate if a hard-copy of the local histology ("path report") report is included and/or if prints are being sent if there is a request for the return.

5 Under the Shipper information, complete all details necessary for the NIDDK Histopathology to return slides to your site.

6 Clearly write the local site's Research Coordinator name and fax in this box so the NIDDK Histopathology Archive can notify your site when materials are received.

*** Some sites may require the blank slides be sent upon return of stained slides, please prepare a new copy of Form 11B and complete as above.**

Form 11B Slide Shipment Manifest –SITE TO NIDDK – Part II

SLIDE SHIPMENT MANIFEST
SITE TO NIDDK

A. OUTGOING: Shaded sections to be completed by the Site Research Coordinator (Shipper). The original form will be maintained in the participant research chart locally. A completed copy of Form 11B will serve as the shipping manifest and should be sent to the NIDDK along with:

1. Requested slides
2. De-identified copy of the local histology report
3. EM prints or disk
4. Form 11C – Stained Slide Return Manifest (reverse)

Mailing address for pathology materials:

Ms. Lisa Swearinger
Kidney Disease Section
10 Center Dr, Room 3N116 NIH
Bethesda, MD 20892-1268

Tel: 301-496-3092
lisas@intra.niddk.nih.gov

Stained Slides		
# Slides Shipped	Date Received	Comments
	1	2
Unstained Slides		
# Slides Shipped	Date Received	Comments
	3	4
EM Images & Pathology Report		
Disk Contents	Report	Disk Received / Date
☐ De-identified Images ☐ De-identified Pathology Report	☐ Indicate here if hard-copy path report enclosed Request for print return? ☐ Yes ☐ No	5 Date Received _____ Comments: _____

Shipper

Coordinator Name: _____ Address: _____
Phone: _____ Address: _____
Fax: _____ City: _____
Shipper Signature: _____ State/Zip: _____

B. RECEIVED: This section is to be completed by the receiver. Upon receipt of pathology packet, completed form should be faxed to research coordinator named above.

Receiver Name (Printed): 6 _____ Date _____
Receiver Signature _____

ATTENTION:

7

FAX:

(Shipper's name and fax here)

Form 11B Slide Shipment Manifest V3.0 FEB-2012

16.C.19.b. *Form 11B/C Slide Shipment Manifest Reference – Part II*

Form 11B/C is a four-part process. Please review all instructions below and document as necessary in Velos.

Form 11B: Upon receipt of the requested pathology materials, the NIDDK should complete the unshaded sections for items shipped as numbered above, and described below. Return these materials (stained slides, prints if requested, and Form C to the local site research coordinator at the address indicated in the "Shipper" section via "Ground" service through the UPS shipping portal (see Appendix N).

Part II. Manifest Form 11B Responsibilities – NIDDK:

1 Please indicate the date stained slides received.

2 Please make any comments as appropriate regarding the condition of the slides, de-identification, or label placement.

3 Please indicate the date unstained slides received

4 Please make any comments as appropriate regarding the condition of the slides, de-identification, or label placement.

5 Please indicate the date compact disk received and any appropriate comments.

6 Please print, date and sign for receipt of shipment materials

7 Please fax Form 11B to the attention of indicated personnel at the respective fax number.

If possible, please return this form with the stained slides when they are shipped back to the institution.

16.C.20. Form 11C Slide Shipment Manifest – NIDDK TO SITE – Part III

STAINED SLIDE RETURN MANIFEST
NIDDK TO SITE

A. OUTGOING Shaded section to be completed by NIDDK (SHIPPER). The original form, with shipping information completed should be sent with the slides to the receiving site in the pre-labeled envelope.

Stained Slides		
# Slides Shipped	**Date Received**	**Comments**
1		
EM Prints (if applicable / requested)		
Prints	**Report**	**Date**
2 □ Yes	3 □ Not applicable	Date Received _____ Comments: _____

Shipper: 4

Name: _____ Address: _____
Phone: _____ Address: _____
Fax: _____ City: _____
Shipper Signature: _____ State/Zip: _____

SLIDE/IMAGE RETURN RECEIPT [SITE]

B. RECEIVED: This section is to be completed by the receiver (Site Research Coordinator).

Receiver Name (Printed): _____ Date _____
Receiver Signature _____

SLIDE/IMAGE RETURN RECEIPT [SITE PATHOLOGY]

This section is to be completed by PATHOLOGY of the originating site indicating return of stained slides (Site research coordinator). The completed form should be maintained in the participant research chart, after entry into the KIDNEY BIOSPECIMEN eCRF.

Pathology Signature: _____ Date _____
Pathology Name (Printed) _____

Form 11C Return Slide Shipment Manifest V3.0 FEB-2012

16.C.20.a. *Form 11B/C Slide Shipment Manifest Reference – Part III*

Form 11B/C is a four-part process. Please review all instructions and document as necessary in Velos.

Form 11C: NIDDK personnel should complete the shaded sections for items being returned to the local site, as described below. Return these materials (stained slides, prints if requested, and Form C to the local site research coordinator at the address indicated in the "Shipper" section via "Ground" service through the UPS shipping portal (see Appendix N).

Part III. Manifest Form 11C Responsibilities – NIDDK

1 Please indicate the number of stained slides being shipped.

2 Please indicate if any prints are being returned, if not, do not mark.

3 Please document if the de-identified report has not been requested.

4 Under the Shipper information, complete all details.

Please return this form with the stained slides when they are shipped back to the institution.

Form 11C Slide Shipment Manifest –SITE TO NIDDK – Part IV

STAINED SLIDE RETURN MANIFEST
NIDDK TO SITE

A. OUTGOING Shaded section to be completed by NIDDK (SHIPPER). The original form, with shipping information completed should be sent with the slides to the receiving site in the pre-labeled envelope.

Stained Slides		
# Slides Shipped	**Date Received**	**Comments**
	1	2
EM Prints (if applicable / requested)		
Prints	**Report**	**Date**
☐ Yes	☐ Not applicable	3 Date Received _____ Comments: _____

Shipper:

Name: _____ Address: _____

Phone: _____ Address: _____

Fax: _____ City: _____

Shipper Signature: _____ State/Zip: _____

SLIDE/IMAGE RETURN RECEIPT [SITE]

B. RECEIVED: This section is to be completed by the receiver (Site Research Coordinator). 4

Receiver Name (Printed): _____ Date _____

Receiver Signature _____

SLIDE/IMAGE RETURN RECEIPT [SITE PATHOLOGY]

This section is to be completed by PATHOLOGY of the originating site indicating return of stained slides (Site research coordinator). The completed form should be maintained in the participant research chart, after entry into the KIDNEY BIOSPECIMEN eCRF.

Pathology Signature: 5 Date _____

Pathology Name (Printed) _____ _____

Form 11C Return Slide Shipment Manifest V3.0 FEB-2012

16.C.20.a. *Form 11B/C Slide Shipment Manifest Reference – Part IV*

Form 11B/C is a four-part process. Please review all instructions and document as necessary in Velos.

Form 11C: Upon receipt of the returned pathology materials, the local site coordinator should complete the unshaded sections for items shipped as numbered above, and described below. Return these materials (stained slides, prints if requested, and Form C to the local site pathology department, obtaining the indicated signature receipt.

Part IV. Manifest Form 11C Responsibilities – Research Coordinator:

1 Please indicate the date stained slides received.

2 Please make any comments as appropriate regarding the condition of the slides or any missing materials.

3 Please indicate the date other returned items received and note any comments.

4 Please print, date and sign for receipt of shipment materials.

5 Return requested items to the local pathology department documenting receiver of materials name, signed and printed, and date. Document this information in Velos, Form 11A-Slides.

16.C.21. Form 13A Follow-Up Participant Information Worksheet

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

FOLLOW-UP PARTICIPANT INFORMATION

Visit: (check one)		4		5		6		7		8		9		10		11		12		13

Healthcare Utilization

	Don't know	# of Times
Since your last study visit, number of times received care in an Emergency Room in a hospital?	4	
Since your last study visit, the number of times seen by a healthcare provider for well/check-up visits (not including this study visit or dental visits)?	5	
Since your last study visit, the number of times seen by a healthcare provider for illnesses/injuries (not including this study visit, dental visits or times when hospitalized overnight)?	6	
Since your last study visit, number of times and total days hospitalized?	7	
AND total # of days:		8

Health Insurance

Since your last study visit, has there been a change in your health insurance? 9		No		Yes		Don't Know	
If yes, now have: (*Check all that apply*)		Private health insurance plan		Medicare/Medicaid			
		Military/VA		None			
10		Other type(s) of health insurance (specify)					
		11					

Social History

Current smoker: 12		Yes (*See Below)		No			
*If Yes: (there are 20 cigarettes in 1 pack)		# of packs smoked a day	13				
		# of years smoking	14				
Pipe or Cigar Use: 15		Yes		No			
Passive smoker (do any of the people who live in the participant's primary household smoke cigarettes, cigars, cigarillos, little cigars or pipes? 16		Yes		No			
Other Drug Use: 17		Yes (specify):				No	
Alcohol Use 18 (*Check only one*)		Daily		3-4 times/week		1-2 times/week	
		1-2 times/month		Less than once/month		None	

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

Socio-Economic Status

19

Since your last study visit, has there been a change in your employment status?		Yes*		No		Don't Know
*If yes, please answer all of the following questions:						
Current employment status: 20		Employed part-time		Employed full-time		
		*Temporarily laid off/on strike		*On temporary medical leave		
		*Permanently disabled		*Retired, not currently working		
		Retired, new career/working		Full-time home maker		
		*Unemployed		Not Applicable		
If not currently employed, last employed:	Month:	21	Year:			

Primary type of work: (*Check only one*) 22		Professional, executive occupation, business owner
		Manager, technical occupation
		Clerical, sales, administrative support occupation, technician
		Skilled labor (e.g. certified electrician, carpenter, welder)
		Semi-skilled labor (e.g. construction help, mechanic's help)
		Unskilled labor (e.g. porters, bell hops, manual labor)
		Homemaker
		Other (specify) 23
		Not Applicable

Since your last study visit, has there been a change in your student status? 24		Yes*		No		Don't Know
*If yes, please answer all of the following questions:						
Current student status: 25 (*Check all that apply*)		Full-time		Part-time		
		Home Schooled		Not enrolled (age eligible)		
		Not enrolled (age ineligible / too young)		Receiving special education services		
				Not Applicable		

Highest grade/level of school completed by participant: (*Check only one*) 26		Too young	
		Kindergarten	
		2nd grade	
		4th grade	
		6th grade	
		8th grade	
		10th grade	
		12th grade	
		2-year associates degree/certificate	
		Master's level diploma	
		Pre-school	
		1st grade	
		3rd grade	
		5th grade	
		7th grade	
		9th grade	
		11th grade	
		High school diploma or equivalent	
		4-year college degree	
		Graduate level diploma (MD, PhD, PharmD, etc.	

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

Since your last study visit, has there been a change in your gross annual household income? 27		Yes*		No		Don' Know	
If Yes, current or expected gross annual household income: 28 (*Check only one*)		$0 - $19,999		$20,000 - $39,999		$40,000 - $59,999	
		$60,000 - $79,000		$80,000 - $99,000		$100,000 +	
		Do not wish to answer				Don't know	

Since your last study visit, has there been a change in 29 the number of Adults (18 and older) in your household?		Yes*		No		Don' Know	
If yes, number of adults (18 and older) in the same household:						30	
Since your last study visit, has there been a change in 31 the number of Children (under 18) in your household?		Yes (See below)		No		Don't Know	
If yes, number of children (under 18) in the same household:						32	

33 Coordinator Signature: _____ Date: _____

34 Coordinator Name (Print): _____

Form 13A Follow-up Participant Info Worksheet v3 Feb-2012 Page 3 of 3

16.C.21.a. *Form 13A Follow-up Participant Information Worksheet Reference*

Header

1 Please enter the participant's initials.

2 Please enter the study visit date.

3 Please enter the Velos ID (e.g. 004021)

Healthcare Utilization

4 Please enter the # of times the participant has received care in an emergency room since the baseline or subsequent follow-up visit (enter 0 if they have not received care in an emergency room over the last 6 months). Check "Don't Know" if the participant cannot recall.

5 Please enter the # of times the participant has been seen by any healthcare provider for well/checkup visits since the baseline or subsequent follow-up visit (enter 0 if they have not been seen over the last 6 months). Do not include dental office visits in this calculation. Check "Don't Know" if the participant cannot recall.

6 Please enter the # of times the participant has been seen by a healthcare provider for sick/injury visits since the baseline or subsequent follow-up visit (enter 0 if they have not been seen for a sickness or injury over the last 6 months). Do not include this visit, overnight hospitalizations or dental visits in the calculation. If the participant cannot recall, check "Don't Know."

7 Please check "Don't Know" if participant can't recall. Otherwise please enter the number of times they were hospitalized since the baseline or subsequent follow-up visit (enter 0 if the participant has not been hospitalized in the last 6 months).

8 Please sum and enter the total number of days the participant was hospitalized in the pasat 6 months.

Health Insurance

9 Please check "Yes", "No", or "Don't Know". If "Yes" please proceed to item 10.

10 Please check all that apply.

11 If "Other type of health insurance" is indicated, please ask the participant to specify and record here.

Social History

12 This question refers to cigarettes. Please answer "Yes" or "No" to the question of current smoker.

13 If "Yes" is checked for current smoker, please ask the participant to estimate the number of packs smoked per day.

14 If "Yes" is checked for current smoker, please ask the participant to estimate the number of years that they have (or they did) smoke.

15 Please check "Yes" or "No."

16 Please check "Yes" or "No."

17 Please check "Yes" or "No." If "Yes" is checked, please ask them to specify the drug(s).

18 Please as the participant to specify alcohol use frequency. If they do not consume alcohol, please check none. Only check one box.

Socio-Economic

19 Please ask the participant if there has been an employment status change since the baseline or subsequent follow-up visit.

If yes, proceed to items 20-23.

20 Provide employment status choices to the participant and check the box accordingly. More than one option may be checked.

21 If participant is not currently employed, please ask them to specify the month and year they were employed last. Enter the month and year of last employment in the spaces provided.

22 Provide primary work type choices to the participant and check the box accordingly. If the participant previously stated that they were unemployed please check N/A

23 If the participant specifies another type of work not listed, please record here.

24 Please ask the participant if there has been a change in student status since the baseline or subsequent follow-up visit. If yes, proceed to items 25-26.

25 If participant is enrolled in school, provide student status choices and check the appropriate box. More than one option may be checked.

26 Check the box with the highest level of education achieved by the participant. Check only one option.

27 Please ask the participant if there has been a change in their gross annual household income since the baseline or subsequent follow-up visit. If yes, proceed to item 28.

28 Please enter the participant's gross annual income. If the participant does not have a gross annual income, enter the gross annual income of the participant's primary residence. If participants ask why you are collecting this information, please refer to the following suggested language:

"*While this is a kidney study, researchers are interested in what can affect your health. Just as race, ethnicity and stress level have been linked to health, researchers have found links between economic status and health outcomes. Remember, this information will not be shared outside of the research staff, and it will not have your name on it. We want to protect your privacy, as well as collect information desired by NEPTUNE researchers."*

29 Consult with the participant to determine if there has been a change in the number of Adults in the household.

30 If the participant indicates a change, document the current number of adults, age 18 or older, living in their primary residence.

31 Consult with the participant to determine if there has been a change in the number of Children in the household.

32 If the participant indicates a change, document the current number of children, age under 18, living in their primary residence.

33-34

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.22. Form 13B Follow-Up Clinical Information Worksheet

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

FOLLOW-UP FAMILY HISTORY INFORMATION

Visit: (check one)		4		5		6		7		8		9		10		11		12		13

Family History of Kidney Disease

4

Since your last study visit, has any family member been diagnosed with kidney disease?		Yes*		No		Don't know
If Yes, which family member(s) (Check all that apply)		Biological Mother				Sibling*
5		Biological Father				Biological Child

* With at least one common parent

6

*IF MORE THAN ONE FAMILY MEMBER HAS BEEN DIAGNOSED, PLEASE MAKE A COPY OF THE FOLLOWING PAGE (PAGE 2) AND COMPLETE FOR UP TO 2 FAMILY MEMBERS. PLEASE BE SURE TO INDICATE WHICH FAMILY MEMBER THE PAGE IS FOR BY CHECKING THE APPROPRIATE BOX AT THE TOP OF THE PAGE.

Form 4B Follow-up Family History Worksheet v3 Feb-2012 Page 1 of 3

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

Family Member: 7		1		2
(Copy this page for an additional family member)				
Which family member (Only check one): 8		Biological Mother		Sibling (with at least one common parent)
		Biological Father		Biological Child

Family Member:

**If yes, please specify disease (Only check one):* 9

	Acute Interstitial Nephritis		Henoch-Schoenlein Purpura (HSP)		Nephrotic Syndrome (unspecified or unknown)
	Acute Renal Failure		Hypertensive Nephropathy (Hypertensive Nephrosclerosis)		Polycystic Kidney Disease
	Acute Tubular Necrosis		IgA-Nephritis		Post-infectious Glomerulonephritis (Infection-related Glomerulonephritis)
	Alport		Infectious/Complement Mediated Glomerulonephritis		Rapidly Progressive Renal Failure
	Amyloidosis		Membrano-proliferative Glomerulonephritis		Renal Dysplasia
	Atheroembolic Disease		Membranous Glomerulopathy (Membranous Nephropathy)		Sarcoidosis
	Chronic Interstitial Nephritis		Minimal Change Disease (Nil Disease)		Thin Basement Membrane Nephropathy
	Chronic Renal Failure (unspecified or unknown)		Monoclonal Gammopathy (Multiple Myeloma)		Thin Basement Membrane Nephropathy
	Diabetic Nephropathy		Nail Patella		Thrombotic Thrombocytopenic Purpura (TTP)
	Focal and Segmental Glomerulosclerosis (FSGS)		Nephritis		Vasculitis
	Hemolytic-Uremic Syndrome (HUS)		Unknown		Other – Specify below*

10 **Other*:** _____

**If additional kidney diseases were diagnosed, please list them here:*

11

Please specify age of onset 12		Years		Don't know

Is there an archived kidney biopsy? 13		Yes		No		Don't know

Is this person on Dialysis? 14		Yes		No		Don't know

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

Family History of Diabetes

Since your last study visit, has any family member been diagnoses with diabetes?	15		Yes		No		Don't know
**If yes, check all that apply*:	16		Biological Mother				
			Biological Father				
			Sibling(s) *(with at least 1 common parent)*				
Number of Siblings with diabetes?	17			Total			Don't Know
Number of biological children with diabetes?	18			Total			Don't Know

Family History of Hypertension

Since your last study visit, has any family member been diagnosed with hypertension?	19		Yes		No		Don't know
**If yes, check all that apply*:	20		Biological Mother				
			Biological Father				
			Sibling(s) *(with at least 1 common parent)*				
Number of Siblings with hypertension?	21			Total			Don't Know
Number of biological children with hypertension?	22			Total			Don't Know

23 Coordinator Signature: _____ Date: _____

24 Coordinator Name (Print): _____

Form 4B Follow-up Family History Worksheet v3 Feb-2012 Page 3 of 3

16.C.22.a. *Form 13B Follow-up Participant Information Worksheet Reference*

Header

1 Please enter the participant's initials.

2 Please enter the study visit date.

3 Please enter the Velos ID (e.g. 004021)

Family History of Kidney Disease

4 Please ask the participant if any family member has been diagnosed with kidney disease since the baseline or subsequent follow-up visits. Check "Yes", "No" or "Don't Know."

5 If yes, check all that apply for family members affected by kidney disease, and if necessary, make an additional copy of the sheet (i.e., both parents affected by kidney disease).

6 If more than one family member has been diagnosed with kidney disease, please make additional copies of Page 2 and complete for up to 2 parents, 2 siblings, or 2 children.

7 Please indicate which family member the worksheet represents by checking the appropriate box at the top of the page.

8 Please indicate the corresponding family member for whom the worksheet represents by checking the appropriate box at the top of the page.

9 Please provide the list of diseases to the participant and check the appropriate box (Only check one box). Please confirm with the patient that the disease was a diagnosis by a medical professional. If the participant is not sure of their mother/father's diagnosis, please check "Unknown." If the disease given by the participant is not listed, please check "Other" and write in the disease name.

Acute Interstitial Nephritis: Nephritis affecting the interstitium of the kidneys and occurring suddenly.

Acute Renal Failure: Rapid loss of kidney function.

Acute Tubular Necrosis: Rapid death of tubular cells (tubule of the kidney). Can present with Acute Renal Failure.

Alport: Genetic disorder characterized by glomerulonephritis, endstage renal disease, and hearing loss.

Amyloidosis: Any condition where amyloid proteins are abnormally deposited in organs and/or tissues.

Atheroembolic Disease: An inflammatory reaction in the small blood vessels of the kidneys.

Chronic Interstitial Nephritis: An ongoing form of nephritis affecting the interstitium of the kidneys.

Chronic Renal Failure (Unspecified/Unknown): Progressive loss of renal function over a period of months or years with no specified cause.

Diabetic Nephropathy: Kidney disease/damage resulting from diabetes complications.

Focal and Segmental Glomerulosclerosis (FSGS): A disease that attacks the kidney's filtering system causing scarring of the tissue.

Hemolytic-Uremic Syndrome (HUS): A syndrome characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. Primarily occurring in infancy and children.

Henoch-Schoenlein Purpura (HSP): A form of blood vessel inflammation that affects the capillaries in the skin and often times the kidneys.

Hypersensitive Nephropathy (Hypertensive Nephrosclerosis): Damage to the kidney due to

chronic high blood pressure.

Iga Nephritis: A form of glomerulonephritis. Also known as Berger's Disease.

Infectious/Compliment Mediated Glomerulonephritis: Acute glomerulonephritis mediated by an infection.

Membrano-Proliferative Glomerulonephritis: Glomerulonephritis caused by deposits in the kidney glomerular mesangium and basement membrane thickening.

Membranous Glomerulopathy: A kidney disorder that involves changes and inflammation of the structures inside the kidney that help filter waste.

Minimal Change Disease (Nil Disease): Nephrotic Syndrome that reveals little or no change in the structure of the glomeruli or surrounding tissues when the kidneys are biopsied.

Monoclonal Gammopathy: Condition where abnormal protein is found in the blood and may progress over decades to other disorders. Also known as MGUS.

Nail Patella: A genetic disorder characterized by small poorly developed nails and kneecaps. Persons with this syndrome may also develop kidney disease. Also referred to as Iliac Horn Syndrome, Hereditary Onychoostedysplasia, Fong Disease, or Turner-Kiser Syndrome.

Nephritis: Inflammation of the kidneys.

Nephrotic Syndrome (Unspecified): A non-specific disorder in which the kidney's are damaged and leaking large amounts of protein.

Polycystic Kidney Disease: A cystic genetic disorder of the kidneys. Also known as PKD or PCKD.

Post-Infectious Glomerulonephritis (Infection Related Glomerulonephritis): Glomerulonephritis as a result of an infection.

Rapidly Progressing Renal Failure: Rapid loss of kidney function which occurs over a few weeks to a few months.

Renal Dysplasia: Abnormal cellular differentiation of the renal tissue.

Sarcoidosis: A multi-system inflammatory disease characterized by small inflammatory nodules. Also known as Besnier-Boeck Disease.

Thin Basement Membrane Nephropathy: Disease characterized by a thinning of the basement membrane of the glomeruli in the kidneys. Also known as Benign Familial Hematuria.

Thrombotic Thrombocyopenic Purpura (TTP): Rare disease of the blood-coagulation system, causing extensice microscopic thromboses to form in blood vessels throughout the body. Also known as Moschcowitz Syndrome.

Vasulitis: Disorder that is characterized by the inflammatory destruction of blood vessels.

10 If "Other" is indicated, please record the affected family member's disease.

11 If afflicted family member was diagnosed with additional kidney diseases, please list them on this line, separated by commas. Only one box should be checked for question 6.

12 Please ask them to specify the age of onset (of afflicted family member's disease)

13 Please ask them if the afflicted family member an archived kidney biopsy.

14 Please ask them if the afflicted family member is on dialysis.

Family History of Diabetes

15 Please check "Yes", "No" or "Don't Know." Confirm with the patient that diabetes was a diagnosis by a medical professional.

16 If "Yes," check all that apply.

17 Indicate the total number of siblings with diabetes, if unknown, check “Don’t Know”.

18 Indicate the total number of children with diabetes, if unknown, check “Don’t Know”.

Family History of Hypertension

19 Please check “Yes”, “No” or “Don’t Know.” Confirm with the patient that hypertension was a diagnosis by a medical professional.

20 If “Yes,” check all that apply.

21 Indicate the total number of siblings with hypertension, if unknown, check “Don’t Know”.

22 Indicate the total number of children with hypertension, if unknown, check “Don’t Know”.

23-24:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.23. Form 13C Follow-Up Clinical Information Worksheet

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

FOLLOW-UP CLINICAL INFORMATION

Visit: (check one)		4		5		6		7		8		9		10		11		12		13

If not previously collected:

	Month	Year
4 **Date of initial presentation of proteinuria/nephrotic syndrome:**		

(please estimate month and year if unknown)

5 **Interval Medical History**

Since your last study visit, have you developed any of the following (Check all that apply):						**If Checked, Month/Year of Onset**
6	Hypertension					7
	Diabetes					
	If checked		Type I		Type II	
	If checked, Requires Insulin		Yes		No	
	Coronary Artery Disease					
	Heart Failure					
	Heart Arrhythmia					
	Stroke					
	Thromboembolic Event					
If checked, Type			Deep Vein Thrombosis		Pulmonary Embolism	
			Embolic Stroke		Renal Artery Disease	
			Renal Vein Thrombosis		Other:	
	Peripheral Vascular Disease					
	Cancer, If checked, type:					
	Rheumatologic Disease, If checked, Type:					

8 **Since your last study visit, have you had any of the following infections (check all that apply):**

	Peritonitis		Sepsis		Cellulitis / Skin Infection
	Pneumonia		Other:		

9	*If any infections were checked, total duration of antibiotic treatment*				*Days*
	If any infections were checked, antibiotic type used (check all that apply):		Oral		Parenteral (IV)
			Topical		Unknown

		Yes	**No**
10	**Since your last study visit, have you contracted Hepatitis?**		
	If Yes, Type: A B C		
11	**Since your last study visit, have you contracted HIV?**		
12	**Since your last study visit, have you received a blood transfusion?**		
13	**Since your last study visit, have you developed any new allergies?**		

Form 13C Follow-up Clinical Info Worksheet v3 Feb-2012 Page 1 of 3

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

14	If yes, Type:	Please specify allergens
	Food	
	Drug	
	Environmental	

15	Was participant pre-pubertal at the last study visit?		Yes		No

	If Yes, please answer the following questions:	Age (Years)	Still Pre-pubertal
16	Age when participant began puberty; e.g., body hair growth (males and females), breast development (females) or deepening of the voice (males)?		
17	Age of participant's first menstrual period?		
		Not applicable (male)	

18 Renal Replacement Therapy History:

Since your last study visit, have you been treated with Dialysis?		Yes*		No
*If Yes, please provide Date started (Month/Year) and Date ended (Month/Year) for up to three treatment series.				Don't Know

19

Series		Start Date (mo/yr)		End Date (mo/yr)		Unknown
	1					
	2					
	3					

20 Since your last study visit, have you received a kidney transplant?				Yes*		No
						Don't Know
If yes:		Month		Year		Unknown

Clinical Symptoms

21 Within the last two weeks has participant had any of the following clinical symptoms?

	Shortness of breath		Swelling		Fever		Chest pain
	Foamy urine		Diarrhea		Nausea and/or vomit		Other

Clinical Nephrotic Exam - Vital Signs and Physical Exam

22

Weight: _____kg (pounds ÷ 2.2 = kg)

Height: _____cm (inches × 2.54 = cm)

Pulse: _____beats/min

Participant Initials: __1___ Visit Date: ____2_____

Patient ID: _____3_____

23

Blood Pressure:

	Right Arm		Left Arm
	Reading:	Systolic	Diastolic
		mmHg	
Seated	1st		
	2nd		
	3rd		
	Average 2nd & 3rd	24	
Standing			

25

Edema Status

Does participant have:	Absent	Present
Periorbital / Facial Edema		
Lower Extremity Edema		
Sacral Edema		
Anasarca (extreme generalized edema)		

26 Coordinator Signature: _____Date:_____

27 Coordinator Name (Print): _____

Form 13C Follow-up Clinical Info Worksheet v3 Feb-2012 Page 3 of 3

16.C.23.a. *Worksheet 13C Follow-up Clinical Information Reference*

Header

1 Please enter the participant's initials.

2 Please enter the study visit date.

3 Please enter the Velos ID (e.g. 004021)

Nephrotic Syndrome Presentation

4 If not previously collected, please ask the participant the date of the initial presentation of their proteinuria and/or nephrotic syndrome. This will not necessarily coincide with the current presentation. Please record in month and year.

5 Interval Medical History: The goal of this section is to capture *changes* since the baseline and subsequent follow-up visits that the participant reports. Please document carefully.

6 These items apply to the participant. Please check the box if participant currently has or has been previously diagnosed with any of the indicated diagnoses.

For Cancer, Diabetes, Rheumatologic Disease, or Thromboembolic Event, please ask "Type" and indicate participant's response by checking the appropriate box.

7 Please indicate the month and year of onset of newly reported diagnoses since prior reports. If checked, please ask the participant to give you the duration of time that has passed since they were diagnosed with the condition (for example, if the participant study visit is 9/2008 and they were diagnosed 3 months ago you would 6/2008) or the year of diagnosis of the condition.

8 Please ask the participant if they were diagnosed for any of the indicated infections since their most recent study visit.

Peritonitis: inflammation of the membrane which lines the abdominal cavity.

Sepsis: inflammation of the entire body (also known as SIRS) and the presence of infection.

9 If any infections were checked, please enter the time in days that they were treated in total and indicate the type of antibiotic used. Check all that apply.

10 Please check "Yes" or "No." If yes is indicated, please specify.

11 Please check "Yes" or "No."

12 Please check all that apply.

13 Please check all that apply.

14 If new allergies have developed, please check all that apply. If any of the allergies are checked, please ask the participant to specify the allergies and list them on the provided lines.

15 Please check "Yes" or "No."

16 Please enter the age in years. Please check "Pre-pubertal" if puberty has not begun.

17 Please enter the age in years. Please check "Pre-pubertal" if participant is female and menses has not begun. Please check "Not Applicable" if participant is male.

Renal Replacement Therapy History

18 Please check "Yes," or "No". If "Yes" proceed to question 19.

19 If "Yes" is checked for question 18, please provide the date started and date ended in months and years. If participant had only one (or only two) treatment series, please leave remaining lines

blank. If treatment is ongoing, please enter start date and leave end date blank. If treatment dates are unknown, please check "Unknown."

20 Please check "Yes," or "No". If "Yes" please obtain all known details.

Clinical Symptoms

21 Check all symptoms that apply

Clinical Nephrotic Exam

22 While participant is at the study visit, please weigh them and record their weight in kilograms (Note: 1lb = 0.45359kg or pounds/2.2 = kg)

While participant is at the study visit, please measure their height and record it in the blank. (Note: 1in = 2.54cm). (Not required for full-grown adult participants).

While participant is at the study visit please take and record their pulse for 30 seconds.

23 While participant is at the study visit, determine from which arm blood pressured will be measured and record. Please refer to the MOP for directions on blood pressure measurement.

Please take and record their blood pressure in both the sitting and standing position. Take the sitting BP three consecutive times (waiting at least 30 seconds after cuff deflation) and record all three measurements.

The standing BP should only be taken once.

24 Average the second and third sitting BP and record the average (this is what should be recorded in Velos).

25 Please examine participant at the study visit and check "Present" or "Absent" for the indicated edemae. For examination directions and edema references please refer to the MOP.

26-27:

*** The person who completes the form with the patient should sign, date and print their name at the bottom of the form.**

16.C.24. [V3] Biobank Specimens Collection Form

Participant Initials: __1___ [V3] Biobank Specimens

Patient ID: _____2_____ Visit Date: ____3_____

[V3] Biobank Specimens Collection- ADULTS & PED

4 **Blood Draw Date:**_____(mm/dd/yyyy)

PROCUREMENT			PROCESSING		Research Coordinator	
Blood Procured?		Y / N 5			Participant fasting?	Y / N 8
Blood draw start time:		6 a.m. / p.m.	Blood processing start time	7 a.m. / p.m.	Hours *NPO: *since last meal/non water beverage	9

Tube Top 10	Tube # 11	Type 12	Blood Procured? 13	# Tubes 14	# Cryovials 15	Please make notes of any aberrations below:
Tiger	19	SST	Y / N		White dot (0 – 1)	16
Purple	14	EDTA	Y / N		Red caps (0 – 2)	
Red	12	RNA PaxGene	Y / N		*Time at room temp* 17 minutes	

18 Prioritization	
1 EDTA, 1 PAXGene required for every visit	Volume of EDTA is less essential than Volume for RNA tube (12)

19 ***Please return this worksheet to the proper Research Coordinator***

Urine MUST be collected prior to biopsy procedure

Spot/Random Clean Catch

Procurement			Processing		
20 Sample Obtained?	Y	N	24 *Unprocessed:*		
21 Date Collected		(mm/dd/yyyy)	# Whole urine aliquots		(0 – 4)
22 Patient Fasting?	Y / N / Don't Know		25 *Empty Samples:*		
23 Sample Collection	a.m. / p.m. / Don't Know		26 # 15 mL tubes		(0 – 2)
			27 # AS Aliquots		(0 – 4)
			28 # AP E (Pellet) Aliquots		(0 – 2)
			29 *PI (Protease Inhibitor) Samples:*		
			30 # 15 mL tubes		(0 – 2)
			31 # AQ Aliquots		(0 – 4)
			32 # AP Q (pellet) Aliquots		(0 – 2)

Packing / Shipping – Outgoing: (to NEPTUNE DACC)

Date Samples Packed (mm/dd/yyyy)	Time Samples Packed	Date Samples Shipped (mm/dd/yyyy)
33	34 a.m. p.m.	35

V3 Biobank Specimens Form Protocol V3.0

16.C.24.a. *[V3] Biobank Specimens Collection Form Reference*

The [V3] Biobank Specimens Collections Worksheet and corresponding CRF should be completed the day of the biopsy or up to one week prior to biopsy. Blood specimens can be obtained pre- (preferred) or post-biopsy procedure if necessary; however, urine specimens MUST be collected prior to biopsy. If a site is unable to obtain urine prior to the biopsy, please collect no sooner than 3 days post-biopsy.

Header

1 Please enter the participant's initials.

2 Please enter the Velos ID (e.g. 004021).

3 Please enter the date V3 biobank specimens are collected.

Blood Procurement and Processing Details

4 Please enter the actual blood draw date. Please note the importance of this as samples for the [V3] can occur pre- (up to 7 days), day-of-biopsy, or post-biopsy (up to 7 days).

5 Record if blood was collected by circling "Y" for yes, or "N" for no for the [V3] biopsy visit.

6 Please enter the time the first blood specimen was obtained and indicate a.m. or p.m.

7 Please enter the time that blood specimen processing began and indicate a.m. or p.m.

8 Please circle "Y" for yes, "N" for no, or DK for "Don't Know".

9 Please enter in the number of hours since the participant has had food or a non-water beverage.

10 Noted here is the color of each vacutainer cap for reference.

11 Number assigned to the respective blood draw tube and in order which draw should occur.

12 Name of corresponding vacutainer used.

13 In relevance to the respective blood tube, circle "Y" for yes, or "N" for no if a sample was procured or not.

14 Please record the number of vacutainers collected for each type.

15 Please record the number of filled cryovials obtained from processing the respective blood tube.

16 Please document any aberrations from the blood MOP in the space provided.

17 Please enter the time the RNA PAXgene tube spent at room temperature in minutes. The tube should sit for 2 hours at room temperature and then be placed in the freezer.

18 Reference this chart for NEPTUNE blood draw prioritizations

19 In case of other laboratory personnel completing this worksheet, it must be returned to the RC.

Spot/Random Urine Procurement and Processing Details

20 Please circle "Y" for yes, or "N" for no if a spot (random or fresh) urine specimen was obtained for the respective study visit.

21 Please enter the date that the random urine specimen was obtained in the format MM/DD/YYYY. Please note the importance of this as samples for the [V3] can occur pre- (up to 7 days), or post-biopsy (up to 7 days). **URINE CANNOT BE COLLECTED POST-BIOPSY DAY OF PROCEDURE.** Day of procedure, pre-biopsy is preferred.

22 Please circle “Y” for yes, or “N” for no. If this information is unknown, please circle “Don’t Know”.

23 Please circle “a.m.” if the random urine was provided during the AM hours, and please circle “p.m.” if the sample was provided during the PM hours. Please circle “Don’t Know” if unknown.

Unprocessed Spot/Random Urine Sample

24 If > 60 mL of a spot/random clean catch urine is obtained, please aliquot 4 unprocessed samples into the whole urine aliquots (‘US’).

Supernatant Samples (Empty): From the empty 15 mL centrifuge tubes, indicate:

25 Line items 26-28 refer to the samples processed from the “Empty” 15 mL centrifuge tubes.

26 Number of “EMPTY” 15 mL centrifuge tubes filled to the 12 mL mark (0-2)

27 Number of spun supernatant Sodium Azide (‘AS’) aliquots (0-4).

28 Number of spun pellet aliquots ‘AP E’ (0-2).

Supernatant Samples from Protease Inhibitor (PI): From the PI 15 mL centrifuge tubes, indicate:

29 Line items 30-32 refer to the samples processed from the “PI” 15 mL centrifuge tubes.

30 Number of “PI” 15 mL centrifuge tubes filled to the 12 mL mark (0-2).

31 Number of spun supernatant ‘AQ’ aliquots (0-4).

32 Number of spun pellet aliquots ‘AP Q’ (0-2).

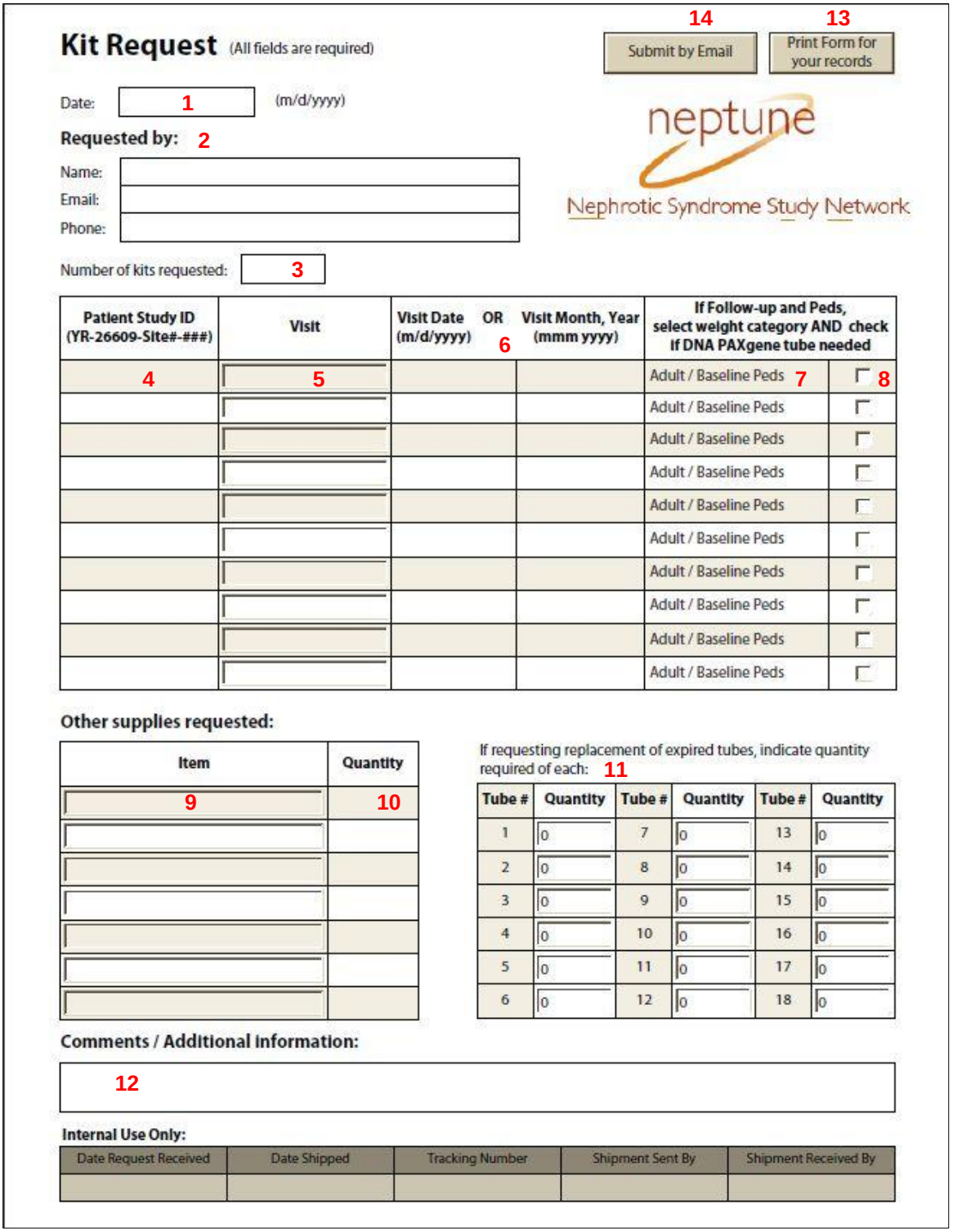
Packing / Shipping (outgoing: to NEPTUNE)

33 When kits are shipped, please document on each V3 biospecimen form the date samples were packed in the format MM/DD/YYYY.

34 Indicate the time each participant kit was packed and circle a.m. or p.m.

35 Record the date the samples were picked up by your local courier in the format MM/DD/YYYY.

16.C.25. Kit Request Form



Kit Request (All fields are required)

14 Submit by Email | 13 Print Form for your records

Date: 1 (m/d/yyyy)

neptune Nephrotic Syndrome Study Network

Requested by: 2

Name:
Email:
Phone:

Number of kits requested: 3

Patient Study ID (YR-26609-Site#-###)	Visit	Visit Date (m/d/yyyy) OR 6 Visit Month, Year (mmm yyyy)		If Follow-up and Peds, select weight category AND check if DNA PAXgene tube needed	
4	5			Adult / Baseline Peds 7	8
				Adult / Baseline Peds	
				Adult / Baseline Peds	
				Adult / Baseline Peds	
				Adult / Baseline Peds	
				Adult / Baseline Peds	
				Adult / Baseline Peds	
				Adult / Baseline Peds	
				Adult / Baseline Peds	
				Adult / Baseline Peds	

Other supplies requested:

Item	Quantity
9	10

If requesting replacement of expired tubes, indicate quantity required of each: 11

Tube #	Quantity	Tube #	Quantity	Tube #	Quantity
1	0	7	0	13	0
2	0	8	0	14	0
3	0	9	0	15	0
4	0	10	0	16	0
5	0	11	0	17	0
6	0	12	0	18	0

Comments / Additional Information:

12

Internal Use Only:

Date Request Received	Date Shipped	Tracking Number	Shipment Sent By	Shipment Received By

16.C.25.a. *Kit Request Form Reference*

The NEPTUNE Kit Request Form should be completed at least one month before the requested kits are needed. In the case of an unexpected visit, a minimum of one week prior is required to ensure delivery and receipt of requested materials.

Basic Information

1 Please enter the date the kit request will be submitted.

2 Please enter your name, email and phone number with extension (if applicable).

3 Please select the **total** number of kits being requested from the drop down list.

Kit Request List

4 Please enter the full participant ID of the first kit being requested in the format YR-26609-Site#--###

5 Please select the required visit from the drop down list.

6 Please enter the expected visit date in the format m/d/yyyy. If not known, please enter the expected visit month in the formation mm/yyyy.

7 Adult or pediatric baseline kit requests: Please leave the drop down as the default choice "Adult / Peds Baseline".

Pediatric follow-up visit kit request: Please select the appropriate weight class from the drop down list. If the participant was enrolled as a pediatric participant and is now over 18, please choose "Peds now over 18" from the drop down.

8 If the kit being requested is for a pediatric participant, please indicate if a DNA PAXgene tube is required. The DNA PAXgene tube should only be collected once per participant during the entire course of the study, unless a redraw is requested.

****Please repeat items 4-8 for any additional kits needed****

Other Supply Requests

9 If other supplies are needed, please select the appropriate choices from the drop down list. If the required supply is not listed, please see #12.

10 Please indicate the quantity of the requested supply that is needed.

11 If replacement blood draw tubes are needed, please indicate the requested number next to the appropriate tube number(s).

Comments / Additional Information

12 Please enter any comments or additional information that is needed with your request. You may also request supplies not listed in the drop down menu for "Other Supply Requests" such as brochures, incentives, or additional NEPTUNE cooler shipping boxes.

Form Submission

13 Once the form is complete, please select the "Print Form for your Records" and save the form for your records.

14 Please choose "Submit by Email" on the top of the form. A pop up window with two options should appear (you may need to disable pop-up blockers). If you use Outlook or another desktop application, choose "Desktop Email Application" and the form will be sent automatically to the

NEPTUNE Biobank. Otherwise, choose “Internet Email” and save the form to your computer and email the saved form to **NEPTUNE-Biobank@umich.edu**.

Receipt of Requested Kits

When sample collection kits are received from the NEPTUNE Biobank, it is each coordinator’s responsibility to fully inspect the contents of the package for completeness and accuracy. Any questions or concerns should be sent to Kyle Spotts at spottsk@umich.edu.

16.C.26. Participant Withdraw Form

neptune

1 Patient Study ID:____ - 26609 - _____ - _____ 2 Participant Initials:_____
3 Visit Number: [V___] 4 Visit Date:_____

PARTICIPANT WITHDRAW FORM

This form must be signed by both the Research Coordinator and the Site Principal Investigator.

Section 1 5

Indicate primary reason for withdrawal:

- ☐ No longer willing to follow the protocol
- ☐ Lost to follow-up (post 4 years)
- ☐ Deceased
- ☐ Other
  *Specify:*_____
- ☐ No longer interested in participating
- ☐ Participant has personal constraints
- ☐ Ineligible after renal biopsy
  *Specify:*_____

6 Date of last visit participant completed prior to premature withdrawal: _____

7 Did the participant request any data and/or specimen(s) be disposed of or autoclaved? (check N/A if participant consented but baseline/biopsy visit not completed)

☐ Yes (specify below) ☐ No ☐ NA

8 If YES selected, please indicate which data and/or specimen(s) the participant wants removed from the NEPTUNE study:

1.	Clinical Data	☐	Yes	☐	No
2.	Serum/Plasma	☐	Yes	☐	No
3.	DNA Samples	☐	Yes	☐	No
4.	Urine	☐	Yes	☐	No
5.	Biopsy tissue	☐	Yes	☐	No
6.	Nails	☐	Yes	☐	No

9 Comments:_____
_____
_____
_____

10 Research Coordinator Signature: _____ Date: _____

11 Research Coordinator Name (please print):_____

12 Principal Investigator Signature: _____ Date: _____

13 Principal Investigator Name (please print): _____

Participant Withdraw Form v2 7/12/2011 Page 1 of 2

1 Patient Study ID:____ - 26609 - _____ - _____ 2 Participant Initials:_____
3 Visit Number: [V__] 4 Visit Date:_____

14 Section 2

If samples are requested to be removed from the NEPTUNE Biorepository, please fax this form, in it's entirety, to the NEPTUNE Data Analysis and Coordinating Center (DACC) at:

NEPTUNE DACC
Fax: 734-615-6005
Phone: 1-877-9-NEPTUNE

15 NEPTUNE DACC:

Please review requested data and/or biospecimen destruction in Section 1 of this form.

16 Data Removal:_____

17 Data fully expunged: ☐ Yes ☐ No (explain below) ☐ NA

18 If No selected, explain:_____

_____

_____

_____

19 Data Manager Signature: _____ Date: _____

20 Data Manager Name (please print):_____

Speciman Removal:

21 Requested specimens destroyed: ☐ Yes ☐ No (explain below) ☐ NA

22 If No selected, explain:_____

_____

_____

_____

23 Biobank Manager Signature: _____ Date: _____

24 Biobank Manager Name (please print):_____

25 Non-NEPTUNE Witness Signature: _____ Date: _____

26 Non-NEPTUNE Witness Name (please print):_____

27 NEPTUNE PI Signature: _____ Date: _____

28 NEPTUNE PI Name (please print):_____

16.C.26.a. *Participant Withdraw Form Reference*

The Participant Withdraw Form Worksheet and corresponding CRF should be completed immediately upon the request of a NEPTUNE participant. Specimens belonging to participants lost to follow-up will remain the property of the biobank until permission is retracted, as indicated in the NEPTUNE Consent template.

Header

1 Please enter the full participant study ID.

2 Please enter the participant's initials.

3 Please enter the Visit Number corresponding to the participant's withdrawal. If the participant is lost to follow-up, enter the subsequent visit corresponding to the last attended study visit. For example, if the last visit attended was [V7], and the participant was not able to be contacted for 4 years, please enter [V8].

4 Please enter the date of withdrawal.

Section 1

5 Indicate the primary reason for withdrawal.

- If the participant has determined they are no longer willing to comply with study procedures, please indicate "No longer willing to follow the protocol".
- If the participant communicates they are no longer available or interested to participate, please check "No longer interested in participating".
- If the study team is unable to contact the participant for > 4 years, please check "Lost to follow-up (post 4 years)".
- If the participant indicates they would still like to participate but are unable to do so (i.e. re-location, change of healthcare and unable to commit to following-up at your site), please check "Participant has personal constraints".
- If the participant has died, please check "Deceased".
- If the participant is determined to have exclusion criteria post-biopsy, please check "Ineligible after renal biopsy" and specify the exact reason in the space indicated.
- If the participant provides an explanation other than listed, please check "Other" and record the reason in the space indicated.

6 Please enter the date of the last completed study visit.

7
- If a participant has requested that any or all of their study-related data and/or specimens be removed from the study, please check "Yes" (see Item 8).
- If the participant has indicated the study has permission to maintain their data and/or specimens, please check "No".
- If the participant is "Lost to follow-up" or "Deceased", please check "NA".

8 If "Yes" was selected for Item 7, please indicate all sample/data types requested to be removed from the Clinical Data bank and the NEPTUNE biobank.

Please be sure to ask the participant specifically for each item type.

9 Please document any study-relevant comments.

10-11: The person who completes the form with the patient should sign, date and print their name at the bottom of the form.

12-13: The local SITE PI must sign, date and print their name at the bottom of the form.

Section 2

14 When samples and/or data are requested to be removed from the study, please fax both pages of the Participant Withdraw Form to the NEPTUNE DACC

- Fax: 734-615-6005
- Phone: 734-615-5021 or Toll Free: 1-877-9-NEPTUNE

NEPTUNE DACC

15 Once the NEPTUNE DACC has received the Participant Withdraw Form, removal of samples and/or data should be completed within 72 business hours.

16 The NEPTUNE DACC must document the actual date of data removal when requested.

17
- If the data is fully expunged from the study database, please check “Yes”.
- If the data is not fully expunged, please check “No” and see Item 18.
- If the participant did not request data to be expunged, please check “NA”.

18 If “No” was selected in Item 17, please describe the reason why this has not been done.

19-20: The Data Manager must sign, date and print their name on these line items.

21
- If the requested specimens were removed from the NEPTUNE Biobank and destroyed, please enter “Yes”.
- If the requested specimens were not removed from the NEPTUNE Biobank and destroyed, please see Item 22 and check “No”.
- If specimen removal is not applicable, please check “NA”.

22 If “No” was checked in item 21, please describe in full why samples have not been destroyed.

23-24: The Biobank Manager must sign, date and print their name on these line items.

25-26: An individual NOT involved in the NEPTUNE study must witness and document the removal and destruction of data and samples.

27-28: The Study PI, Matthias Kretzler, M.D., must sign, date and print their name on this form.

NEPTUNE DACC: Please fax this document to initiating site upon completion of request.

17. Appendix D. Suggested Screening Language

*** RC should have screened for items on PART I of Eligibility WORKSHEET in advance of eligibility questions for potential participant ***

Suggested Screening Language:

This is a study for Nephrotic Syndrome which includes FSGS, MCD, and MN. You qualify as a potential participant because you are *already* getting a renal biopsy. We would ask for your permission to obtain some additional renal tissue from that procedure, in addition to some blood and urine. We would like to collect blood and urine over the course of the study.

This study may require additional time or visits to [Healthcare facility]. Initially, there will be 13 total visits (year 1: every 4 months, years 2-5: every 6 months).

We would also ask for you to complete some questionnaires during some of the study visits and provide nail clippings.

Would you be interested to see if you are eligible to participate?

Would you be willing to sign an informed consent agreeing to be in the study after learning more about the study details?

18. Appendix E. Physical Measurements

18.A. Height

Height Measurement

Using a clinic stadiometer or infantometer, usually attached to the clinic scale, obtain participant's height, without shoes. Record the height in centimeters (cm) on the worksheet.

1 inch = 2.54 cm

18.B. Weight

Weight Measurement

Using a clinic scale, obtain the participant weight (without shoes) in pounds or kilograms and record the result on the worksheet. If the weight is obtained in lbs, convert the result to kg and record this on the worksheet as well.

1 lb = 2.2. kg

18.C. Blood Pressure

18.C.1. General Information

In this section, step-by-step procedures for blood pressure measurement will be presented. Please be sure to follow the procedures outlined below unless exceptional circumstances arise. If, and when, these circumstances arise please seek a Blood Pressure Consultant, so that participants will be appropriately evaluated. Blood pressure will be measured at the Baseline Visit, and at every Follow Up Visit. You will record blood pressure results on the Baseline Clinical Information and Follow Up Clinical Information Worksheets, as well as on the coordinating Velos Case Report Forms.

Preparation for Blood Pressure Measurement

Participants should abstain from caffeine, smoking, and exercise at least one-half hour prior to and until completion of the blood pressure measurement. Currently prescribed medications, including those affecting blood pressure and non-prescription drugs, should be recorded on the Concomitant Drug Log (Form 5) and in Velos.

Participants should be given full explanation and instructions about the preparation for the blood pressure examination and an opportunity for brief questions. Blood pressure measurement should take place in a separate, quiet room where no other activity is taking place, and where temperature fluctuations are minimal. Scheduling procedures should try to establish consistent appointment times to minimize as much as possible the impact of daily blood pressure variation. Equipment being used should be calibrated by local institutional standards and made ready for use prior to the appointment. Arm measurement, cuff selection and placement should be completed prior to a five minute rest period in this quiet room. Explain to the participant that the five-minute rest period will provide for more valid blood pressure measurements. Preferably, at this time, the

observer should leave the room. The participant should be relaxed, seated with back supported with legs uncrossed and feet comfortably flat on the floor, not dangling. The participant should be instructed to refrain from using a cell phone. An aneroid sphygmomanometer is the preferred standard equipment for all blood pressure measurements at each NEPTUNE study visit. We recommend that this device is calibrated at the initiation of the study and annually according to sites' local institutional policies.

An appropriate electronic blood pressure device may be used in place of the aneroid sphygmomanometer in the place of untrained clinical staff. Please use the device according to the manufacturer's instructions.

Arm Measurement and Cuff Sizes

The proper cuff size should be used to avoid under- or over-estimating the correct blood pressure. To determine the proper cuff size, please follow the procedures outlined below:

- Measure the arm circumference at the midpoint of the arm at each visit.
- Take the measurement on the right arm which has been bared from the shoulder.
- With the participant standing, holding the forearm horizontal (90 degree angle), measure the arm from the acromion (or boney extremity of the shoulder girdle) to the olecranon (or tip of the elbow) with a plastic coated metric tape.
- Mark the midpoint on the dorsal surface of the skin.
- Ask the participant to relax their arm straight down along the side of their body.
- Measure the circumference of the arm by drawing the metric tape snugly around the arm at the level of the midpoint marking. **Make sure the tape is kept horizontal and do not wrap it so snugly that it indents the skin.**
- Using the measurement obtained, consult the chart below to determine cuff size. Try to use the same cuff size for every measurement taken from that particular participant.
- Do not use the cuff itself as a measurement device and refer to the chart below for every cuff size determination.

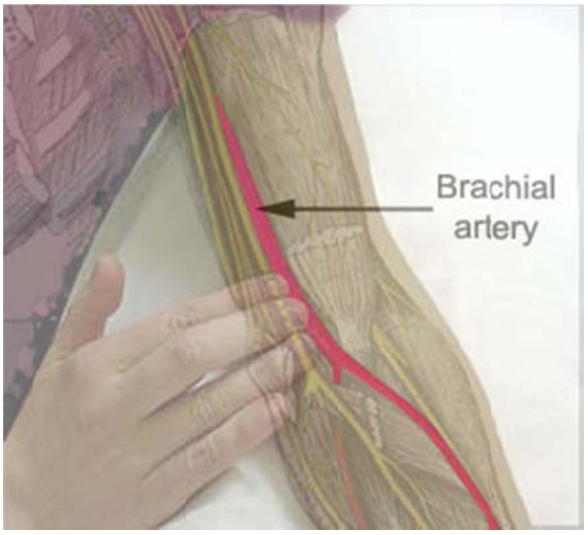
Arm Circumference	**Cuff Size (cm)**
< 24 cm	Child, Small Adult
24.0 to < 33.0 cm	Adult, Regular
33.0 to 41.0 cm	Large Adult
< 41.0 cm	Thigh, Extra Large

Applying the Blood Pressure Cuff

To ensure correct placement of the blood pressure cuff, please follow the steps below:

- Ask the participant to remove any outer clothing and roll up their sleeve so that the area where the cuff will be applied is bare.

- Seat the participant with their elbow and forearm resting comfortably on a table with the palm of their hand turned upward.
- Fold the cuff bladder (the inflatable portion of the blood pressure cuff) in half mating each corner of the bladder to find and mark the midpoint on the cuff cover with a piece of tape or pencil.
- Locate the brachial artery is located by palpation and place the cuff around the upper right arm so that the piece of tape (on the cuff) lies over the brachial artery and the mid-height of the cuff is at heart level. The lower edge of the cuff should lie about 1 inch above the natural crease in the center of the arm.

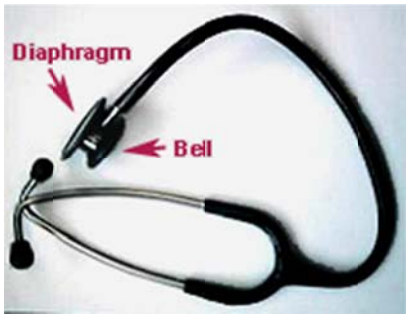


http://www.medicine.mcgill.ca/physio/vlab/cardio/back.htm

The brachial artery is usually located above the crease of the arm, slightly toward the body.

- Wrap the cuff snugly around the arm, with the palm of the participant's hand turned upward, and lock the fabric fastener.

Stethoscope



http://www.medicine.mcgill.ca/physio/vlab/cardio/back.htm

A standard Littman stethoscope (or other comparable stethoscope) with a bell should be used. Stethoscope tubing should be about 12 to 15 inches from the bell piece to "Y"

branching. This length provides optimal acoustical properties and allows the observer to easily read the sphygmomanometer. Please refer to the following when using the stethoscope:

- Place the ear pieces into the external ear canal. The ear pieces should be tight enough to exclude outside sound but not so tight that they cause discomfort.
- Turn the valve, between the bell and the diaphragm, in the direction of the bell.
- Applying light pressure, place the bell of the stethoscope on the skin over the brachial artery, immediately below, but not touching, the cuff.

18.C.2. Blood Pressure Measurement Step By Step

If a trained clinician is unavailable to perform the blood pressure measurement, sites should follow the local institutional policy for obtaining blood pressure with either an aneroid sphygmomanometer or electronic blood pressure measurement equipment locally available.

Provided below are suggested guidelines to determine blood pressure measurement:

Determining the Peak Inflation Level

Determine the Peak Inflation Level for the participant:

- Attach the cuff tubing to the aneroid sphygmomanometer.

http://www.mystethoscope.com/imagemagic.php?img=3Nra2tLsorm%2Fxt3h2rXL0p6n3d3g&w=300&h=368&page=prod_info

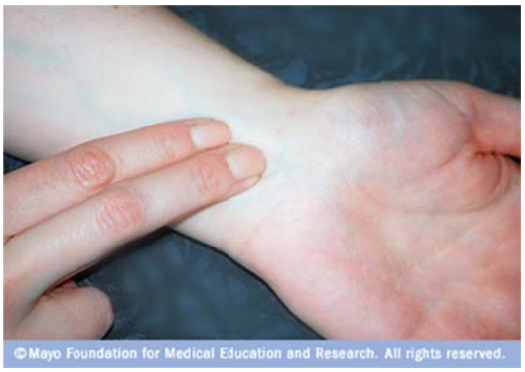
- While palpating the pulse, observe the sphygmomanometer and inflate the cuff rapidly to 60 mmHg and then slowly inflate in increments of 10 mmHg until the pulse is no longer felt. If the pulse is still felt, the cuff pressure should be increased until the pulse disappears. The pressure at which the pulse is no longer heard is called the Observed Pulse Obliteration Pressure. Record this value on the worksheet.
- After the Pulse Obliteration Pressure has been determined, quickly and completely deflate the cuff.
- Add 30 mmHg to the Pulse Obliteration Pressure. This summed value is the Peak Inflation Level (this is the level that the cuff should be inflated to for all readings). Record this value on the worksheet. For example: If the Pulse Obliteration Pressure is 80 mmHg, the Peak Inflation Level would be 110 mmHg.

NOTE: All readings on the sphygmomanometer are made to the nearest even digit. Any reading that appears to fall exactly between markings on the column should be read as the marking immediately above, i.e., 2, 4, 6, 8, or 0.

18.C.3. Pulse Measurement

Determine the pulse of the participant:

- Palpate the radial artery on the participant's wrist. Use the participant's right arm for both pulse and blood pressure measurements. If this is not possible, use the left arm. Document which arm is used to measure pulse and blood pressure on the worksheet.



- Ask the participant to sit quietly with their feet flat on the floor, in an erect but comfortable posture for at least five minutes prior to pulse measurement.
- Place the participant's elbow and forearm comfortably on a table with the palm of their hand turned upward.
- Using a stopwatch, count the participant's pulse for exactly 30 seconds and record.
- Multiply this number by 2 and record the product as the heart rate (beats per minute) on the worksheet.

NOTE: Make note of any irregularities observed and notify the Principal Investigator.

18.C.4. Blood Pressure Measurement Procedures (Seated)

The seated blood pressure should be measured three times at each clinic visit. Record all three readings on the Worksheet (the average of the second and third measurements will be recorded on the CRF). Blood pressure equipment should be checked prior to seeing the participant. Once a participant has sat quietly for at least five minutes and Peak Inflation Level and pulse have been determined, blood pressure measurements may be taken. Please follow the instructions below for blood pressure measurement procedures:

- All blood pressure readings taken for the NEPTUNE Study should be performed by trained clinical or research staff at NEPTUNE Study Clinics or satellite offices.
- All blood pressure measurements should be taken using the aneroid Sphygmomanometer.
- Connect the cuff to the aneroid sphygmomanometer device.
- Place the ear pieces of the stethoscope into the ears.

- Apply the bell of the stethoscope over the brachial artery, just below, but not touching the cuff.
- Using the previously determined peak inflation level, rapidly inflate to this level.
- Deflate the cuff, by adjusting the valve, at a constant rate of 2 mmHg per second, listening carefully.
- Note the pressure where the first of two consecutive beats are heard. This is the systolic reading. Record this pressure on the worksheet.
- Note the pressure where the last of two consecutive beats are heard. This is the diastolic reading. Record this pressure on the worksheet.
- Continue deflating until 10 mmHg past the diastolic reading.
- Open the valve to completely deflate and disconnect the tubing.
- Remove the stethoscope earpieces from the ears.
- Repeat the previous steps two more times, taking a total of three blood pressure measurements. Make sure to wait at least 30 seconds after deflation of the cuff prior to re-inflation. Record all three BP measurements on the Worksheet (Baseline Clinical Information [4C] or Follow-Up Clinical Information [13C]. Average the second and third readings and record the Average on the Case Report Form.
- Finally, raise the participant's arm overhead for 15 seconds without the participant's assistance. The arm should be fully supported at the elbow and wrist by the RC and the participant should not help to support the raised arm.

Notes on Determining Systolic and Diastolic Blood Pressure:

Control of the deflation rate is essential for accurate readings. The aneroid dial (pressure dial) should drop at 2 mmHg per second from the maximum pressure until it has dropped 10 mmHg below the last regular sounds can be heard. The systolic value can be identified as the pressure level where the first of two or more consecutive beats are heard in an appropriate rhythm. The diastolic value can be identified as the pressure level where the last two or more consecutive beats are heard.

18.C.5. Standing Pulse and Blood Pressure Measurement

- After completing 3 seated blood pressure readings, raise the bedside table at the participant's immediate right so that unnecessary movement or walking will not occur when the participant is asked to stand.
- Ask the participant to stand quietly with their arms relaxed at their sides for 2 minutes.
- After 2 minutes, raise the participants arm (fully supported overhead) for 15 seconds.
- Place the participant's arm on the bedside table with the palm of the hand turned upward. The bedside table needs to be elevated so the arm can rest at heart level for the standing pulse and blood pressure. If the table can not be elevated to that height, pillows can be added to the table top to bring the arm to heart level.
- Immediately following, palpate the radial artery and count the participant's pulse for thirty seconds. Multiply by two and record the participant's hear rate, in beats per minute, on the case report form.
- Take one standing blood pressure measurement, as described above, and record the values on the worksheet and later on the case report form.

Forgotten Blood Pressure Readings

If for any reason the observer is unable, or has forgotten, to complete any portion of the exam, and the participant is gone, leave the items blank on the worksheet.

If a blood pressure value is missed or forgotten, during the blood pressure reading procedure, completely deflate the cuff and start over with a replacement reading after 30 seconds.

Do not re-inflate the blood pressure cuff during a reading and do not repeat a reading just because the measurement looks unusual to you.

Reporting the Blood Pressure Results to the Participant

If the participant would like to know his or her blood pressure results, average the second and third systolic readings, and second and third diastolic readings, and give these results to the participant.

18.C.6. Edema Assessment

General Information

At baseline and follow up visits RCs will be asked to assess the presence of edema for the participant. In this section, step-by-step procedures for assessment of edema will be presented. Please be sure to follow the procedures outlined below.

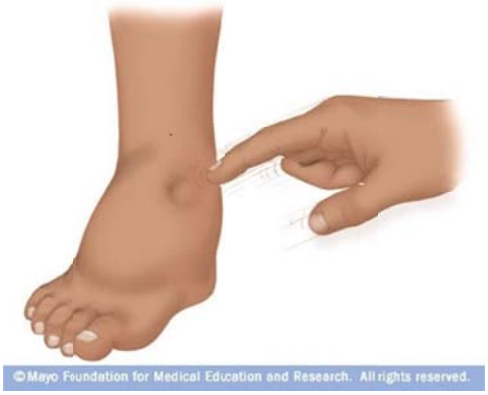
Edema Overview

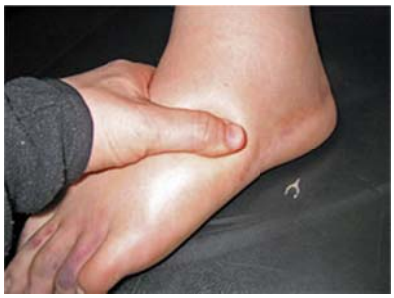
Edema is the swelling of tissues as a result of excess water accumulation. This swelling can occur in a single area on the body, including around the eyes (periorbital edema), in the lower back (sacral edema), in the legs (lower extremity or peripheral edema), or all over the body (anasarca). The NEPTUNE Study is interested in capturing both isolated and generalized edema.

Edema Assessment Step by Step

Please follow the step-by-step instructions below for participant edema assessment.

Lower Extremity Edema Assessment





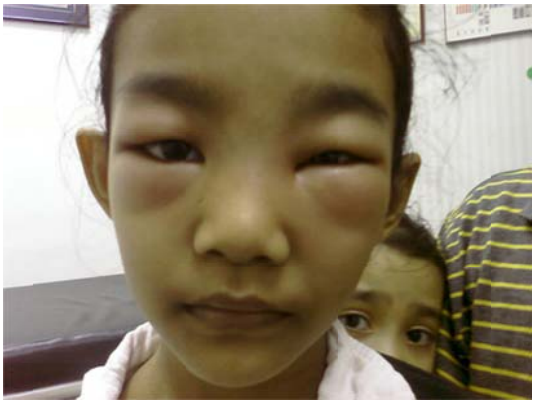
(Reference http://www.ehow.com/how_5607991_test-ascites.html

- Ask the participant, or their legal representative, if they have noticed significant swelling in their legs and whether or not this swelling is currently present.
- Looking at the participant, do both legs appear uniform?
- Looking at the participant, does the skin on the legs appear red, tight, glossy, or swollen?
- Perform a pit test.

Pit Test

- Press firmly on lower extremity below the knee (foot, ankle, or pre-tibial area) with your finger for 10-20 seconds.
- After 10-20 seconds stop pressing, remove your finger, and check for a persistent depression in the skin.
- If a depression, or "pit", is present, the participant is positive for lower extremity edema.
- Please check "Yes" on the worksheet and Case Report Form.
- If the RC is unsure, please consult a physician.

Periorbital Edema Assessment



- Ask the participant, or their legal representative, if they have noticed significant swelling around their eyes and whether or not this swelling is currently present.
- Does the participant's eye or eyes appear significantly swollen? If so, the participant is positive for periorbital edema.
- If the participant is positive for periorbital edema, please check "Yes" on the worksheet and Case Report Form.
- If the RC is unsure, please consult a physician.

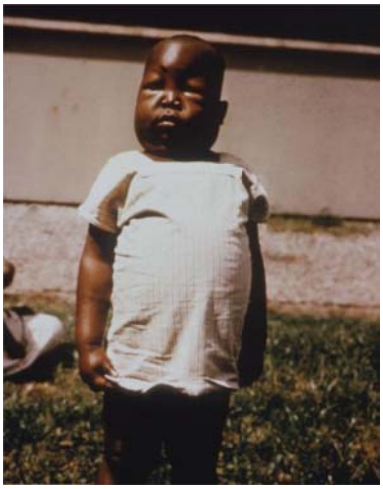
Sacral Edema Assessment

- Ask the participant, or their legal representative, if they have noticed pronounced swelling around their lower back and whether or not this swelling is currently present.
- Looking at the participant, does the skin on the lower back appear red, tight, glossy, or swollen?
- Perform a pit test.

Pit Test

- Press firmly on the sacral area with your finger for 10-20 seconds.
- After 10-20 seconds stop pressing, remove your finger, and check for a persistent depression in the skin.
- If a depression, or "pit", is present, the participant is positive for lower extremity edema.
- Please check "Yes" on the worksheet and Case Report Form.
- If the RC is unsure, please consult a physician.

Anasarca Assessment



http://commons.wikimedia.org/wiki/File:Plasmodium_falciparum_nephrosis_edema_PHIL_3894_lores.jpg

- Does the participant have swelling in many areas (the face, hands, extremities, torso)? This is considered to be generalized edema or anasarca.
- Perform a pit test on upper extremities, thighs, abdomen.
- If the participant has edema in the upper and lower extremities, torso, and/or face, this participant has anasarca. Please check "Yes" for anasarca on the Worksheet and Case Report Form in addition to the individual areas of edema.
- If the RC is unsure, please consult a physician.

20. Appendix G. Nail Clippings

20.A. Collection of Nail Clippings

General Information

Data collection of fingernail clippings will occur at baseline and annually. Record information on the Biospecimen Worksheets [Forms 8 and 14] and transfer to the Biospecimen CRF within one week of study visit.

The nail clippers used must be 100% stainless steel to prevent metal contamination of the nail clippings.

Supplies:

- The nail clipper used to collect these specimens should be made of 100% stainless steel not containing any trace metals.
- NEPTUNE Study ID-labeled coin envelopes for storage (provided in the baseline and annual kits)

20.A.1. *Instructions for Nail Specimen Collection*

- Collection of fingernails is preferred. Toenail clippings are to be obtained only when participant cannot provide fingernail clippings.
- It is recommended that the participant provide the nail clippings during the clinic visit. If this is not possible, the participant can collect their clippings at home and bring them to the next scheduled study visit or as arranged by the local research coordinator. Participants may have their nails clipped by a doctor, podiatrist, manicurist, etc, in advance of their scheduled clinic visit, and bring the clippings with them to the visit; but it should be communicated there is no specific reimbursement for this preference.
- Participant will be instructed to remove all nail polish prior to the clinic visit. During the clinic visit, each participant may clip their own fingernails. They are to clip all 10 fingernails. The amount of clipping obtained should be approximately one millimeter from each nail.
- Research Coordinator or participant will place their fingernail clippings directly into the coin envelopes.
- If participant cannot provide fingernail clippings, they should be instructed to clip their toenails to obtain the required specimen. They will place the toenail clippings into the envelope and give the envelope to the study coordinator.

20.A.2. *Storage of Nail Clippings*

- The study coordinator will store the coin envelopes containing the nail specimens in a dry, cool space.
- Coin envelopes are pre-labeled with the participant ID number and the visit number No other participant identifiers should be recorded on the envelope.
- Record the Nail Specimen details in the biospecimen worksheet and transfer to the Velos case report form for that clinic visit.

20.A.3. *Additional Considerations*

- It is preferred that participants do not wear nail polish on the data collection visit; however, painted nail clippings will be accepted.

- Acrylic nails are not acceptable. The participant should be asked to provide toenail clippings instead.
- Other nail treatments such as Nail Glue or Nail Strengtheners are acceptable.
- If the participant has nail fungus or discoloration, he/she may provide specimens unless the procedure causes pain or discomfort.
- If the participant cannot clip all ten nails, he/she should try to clip as many nails as possible. If the participant has very short fingernails and cannot clip at least one millimeter, we would prefer they take the clippings at the next study visit when the nails have grown. If the participant has a few long nails, they may clip a large amount of one nail, rather than a small amount of each nail. The participant can clip both his/her fingernails and toenails in order to get a total of 10 nails.

20.A.4. *Instructions for Shipping of Nail Specimens*

- Periodic shipping of the nail specimens to the NEPTUNE Biorepository will be conducted by the study coordinator.
- These specimens ***SHOULD NOT*** be shipped on dry ice with the corresponding samples.
- These specimens can be shipped with regularly scheduled shipments *outside* the dry ice box (between the cardboard and lid are preferred).
- The manifest should include the nail specimens.
- Nail specimens will be shipped annually from each site.

19. Appendix F. Quality of Life Questionnaires

19.A. PedsQL™ Administration Guidelines℠

The following guidelines are intended for use by individuals trained in the administration of standardized questionnaires. The PedsQL™ administrator is crucial in developing rapport with the respondents, emphasizing the importance of the questionnaire, addressing concerns, and ensuring that the PedsQL™ is completed accurately and confidentially.

19.A.1. General Protocol

1. The parent/child should first complete the PedsQL™ Generic Core Scales and then complete any additional PedsQL™ Module.
2. Parents, Children (8-12) and Teens (13-18) may self-administer the PedsQL™ after introductory instructions from the administrator. If the administrator determines that the child or teen is unable to self-administer the PedsQL™ (e.g., due to illness, fatigue, reading difficulties), the PedsQL™ should be read aloud to the child or teen. For the Young Child (5-7), the PedsQL™ should be administered by reading the instructions and each item to the young child word for word. At the beginning of each subscale repeat the recall interval instructions (one month or 7 days) to remind the young child to respond only for that specific recall interval. Use the separate page with the three faces response choices to help the young child understand how to answer. When reading items aloud to a child, intonation should be kept neutral to avoid suggesting an answer.
3. If a child has difficulty understanding the age-appropriate PedsQL™, the preceding age group version may be administered to the child (e.g., administering the Young Child (5-7) Self-Report version with the three faces response choices to an 8 year old). However, if a child presents with severe cognitive impairments (as determined by the administrator), the PedsQL™ may not be appropriate for that child. In such cases, only the Parent-Proxy Report should be administered to the child's parent.
4. The parent and child must complete the questionnaires *independently* of one another. Discourage the parent, child, or other family members from consulting with one another during the completion of the questionnaire. Let them know that they can feel free to discuss their answers following completion of the questionnaires, but that it is important to get both the parent's and the child's *individual* perspectives. If you are administering the questionnaire to the child, the child should be facing away from the parent.
5. If the child or parent has a question about what an item means or how they should answer it, do not interpret the question for them. Repeat the item to them verbatim. Ask them to answer the item according to what *they think the question means*. If they have trouble deciding on an answer, ask them to choose the response that comes closest to how they feel. The child and/or the parent has the option of not answering a question if they truly do not understand the question.
6. If a parent/child asks you to interpret the responses, tell her/him that you are not trained to interpret or provide a score for the answers given. If the PedsQL™ is being used for a clinical study, let the parent/child know that their answers will be combined with other participants' answers and analyzed as a group rather than as individual respondents.
7. Document all reasons for refusals and non-completions of the PedsQL™.

19.A.2. Administering the PedsQL™

1. The following scripts have been developed as a guide to introduce the PedsQL™ to the child and his/her parent(s). Modify the language to a style that is most appropriate for you and the respondent.

For the child:

The PedsQL™ asks you questions about how you feel and what you think about your health. It is not a test, and there are no right or wrong answers. It takes about 5 minutes to complete. If you have any questions, please let me know.

For the parent:

The PedsQL™ is a questionnaire that assesses health-related quality of life in children and adolescents. It contains questions about your child's physical, emotional, social, and school functioning ***in the past one month (****or for the Acute version****, in the past 7 days)****.*

The PedsQL™ is brief and typically takes less than 5 minutes to complete. It is not a test, and there are no right or wrong answers. Please be sure to read the instructions carefully and choose the response that is the closest to how you truly feel. Please do not compare your answers with your child's responses. We are interested in your and your child's ***individual*** *perspectives. However, feel free to discuss the questionnaire with your child* ***after*** *you have both completed it and returned it to me. If you have any questions, please let me know.*

2. Provide the respondent with a pen or pencil and a solid writing surface. If a table is not available, the participant should be provided with an item such as a clipboard. Remain nearby should questions or concerns arise.
3. When the parent/child returns the PedsQL™, look it over and check to see that all answers have been completed. Verify that no item has more than one response. If any responses are incomplete, illegible, or there are multiple responses for an item, please ask the parent or child to indicate their response.
4. Ask the participants if they had any difficulties completing the questionnaire or if they have any other comments regarding the questionnaire. Document any important feedback.
5. Thank the parent and child for taking the time to complete the questionnaire. If the study design involves following up with these respondents, let them know that they may be asked to complete the PedsQL™ again at another time. Indicate when they can expect to be contacted again if known.

19.A.3. Study Documentation

The completion or non-completion of the PedsQL should be documented in Form 6A-E and the corresponding CRF. Please review 16.C.11 for documentation instructions.

19.B. SF-36™

19.B.1. Adult Population

This Quality of Life assessment is administered to adult participants only (ages 18+).

19.B.2. General Protocol

The instructions can be read to a participant, or the participant can read the instructions at the top of the survey. Please provide your participant a pencil to complete the survey.

The SF-36 questionnaire will serve as the study source documentation and should remain in the on-site study chart, dated and signed at the completion of the visit.

Instructions for completing the questionnaire: Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by filling in the bubble that best represents your response.

19.B.3. Study Documentation

The completion or non-completion of the SF-36 should be documented in Form 6A-E and the corresponding CRF. Please review 16.C.11 for documentation instructions.

19.C. PROMIS – Patient Reported Outcomes Measure Information System

The following instructions are to aid the site investigators and the research coordinators in administration of the Patient Reported Outcome Measurement Information System (PROMIS) in NEPTUNE cohort participants. All NEPTUNE participants, age 8 and above, who are English-speakers, are to be administered the PROMIS survey.

19.C.1. PROMIS Registration

NEPTUNE Research Coordinators must complete registration before entering NEPTUNE participants into the PROMIS Assessment Center. Please contact the NEPTUNE Data Manager, Ellen Woodard at erhw@umich.edu if you did not complete the PROMIS registration during the training period.

Access must be granted by the Data Manager prior to completing the registration.

19.C.1.a. *PROMIS Assessment Center Registration (Research Coordinator)*

Please see pages 4-5.

19.C.1.b. *PROMIS Assessment Center Registration (Participant)*

Please see pages 6-9.

19.C.2. Survey Execution and Data Collection

In order for survey administration to be successful, there must be consistent, uninterrupted access to the internet.

Access the study website using any web browser:

https://www.assessmentcenter.net/ac1/Assessments/NEPTUNE

This website will be used each time the survey is completed so it is recommended that shortcuts be placed on each computer desktop to facilitate navigation.

Participants may complete the PROMIS survey outside the study visit, by being provided the study web link and their Participant User ID and Password (recorded and stored for subsequent study visits on Form 7 by the site research coordinator).

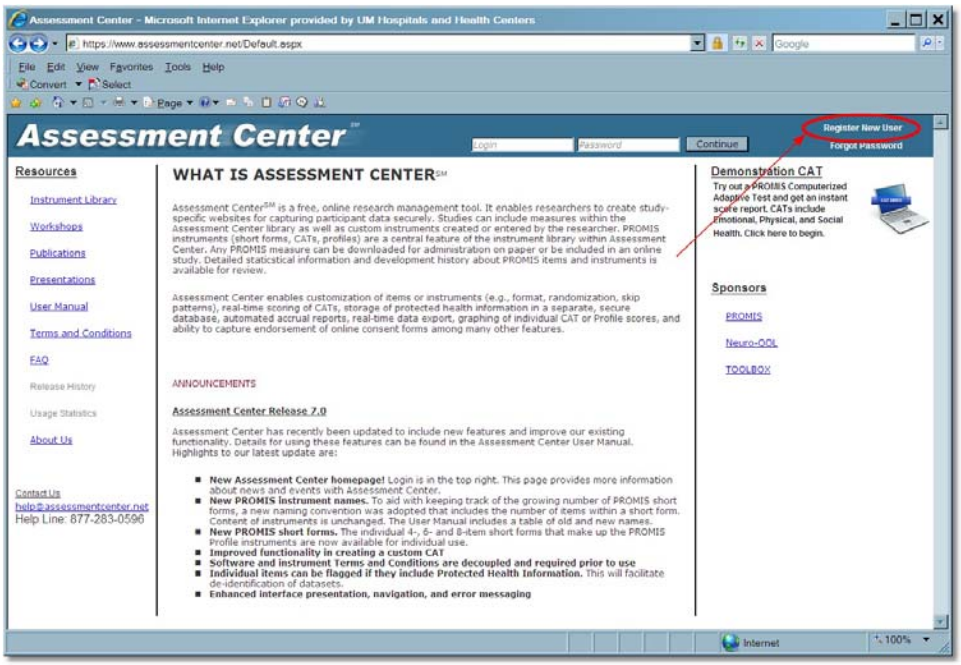
19.C.3. Study Documentation

The completion or non-completion of the PROMIS should be documented in Form 7 and the corresponding CRF. Please review 16.C.11 for documentation instructions.

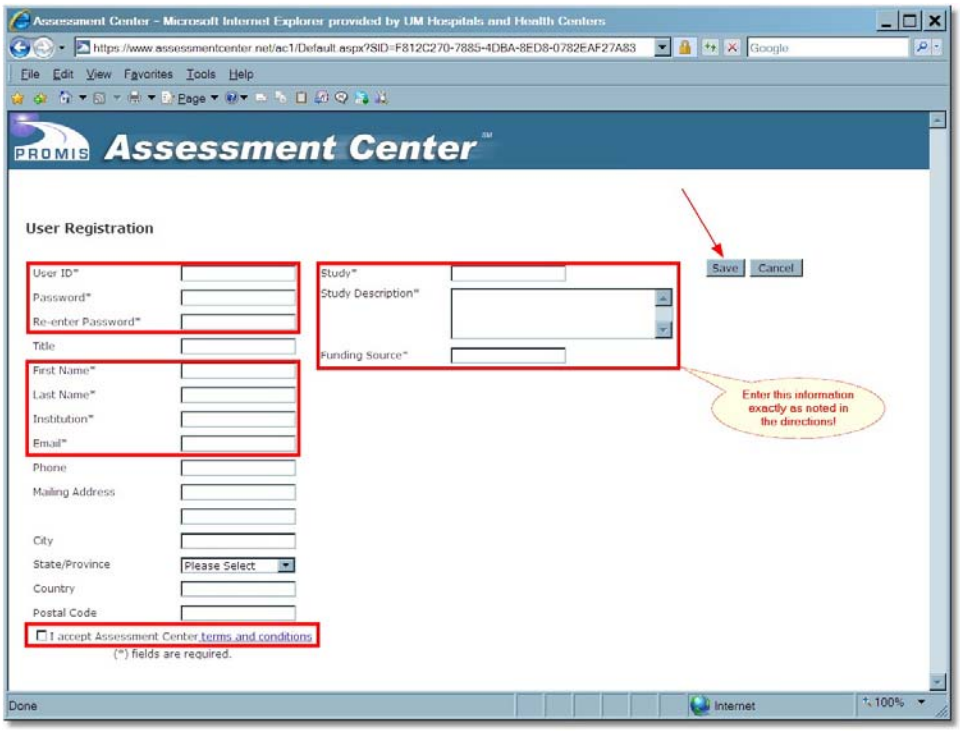
PROMIS Assessment Center

Study Coordinator Registration

1. Go to the Assessment Center web page – www.assessmentcenter.net/ac1 - and click on the "Register New User" link.



2. Complete all fields marked with an asterisk (*).



Make special note of the following:

a. Your password must be at least six (6) characters and can be any combination of letters, numbers or special characters.

b. If another user has already registered with the same combination of last name, first name and institution, you must change at least one of these registration elements.

c. You **MUST** click the box to accept the Assessment Center terms and conditions.

d. Enter EXACTLY the following in the "Study," "Study Description" and "Funding Source" fields:

- Study – NEPTUNE
- Study Description – The Nephrotic Syndrome Study Network is investigating Focal Segmental Glomerulosclerosis, Minimal Change Disease, and Membranous Nephropathy
- Funding Source – NIDDK, ORDR, NephCure Foundation, Univ of MI

3. Click the "Save" button.

To finalize your registration, go to https://www.assessmentcenter.net/ac1/Default.aspx and log in using the User ID and password you specified during the registration process. You can then log right back out again. (**Do NOT skip this step or your registration will be incomplete!**)

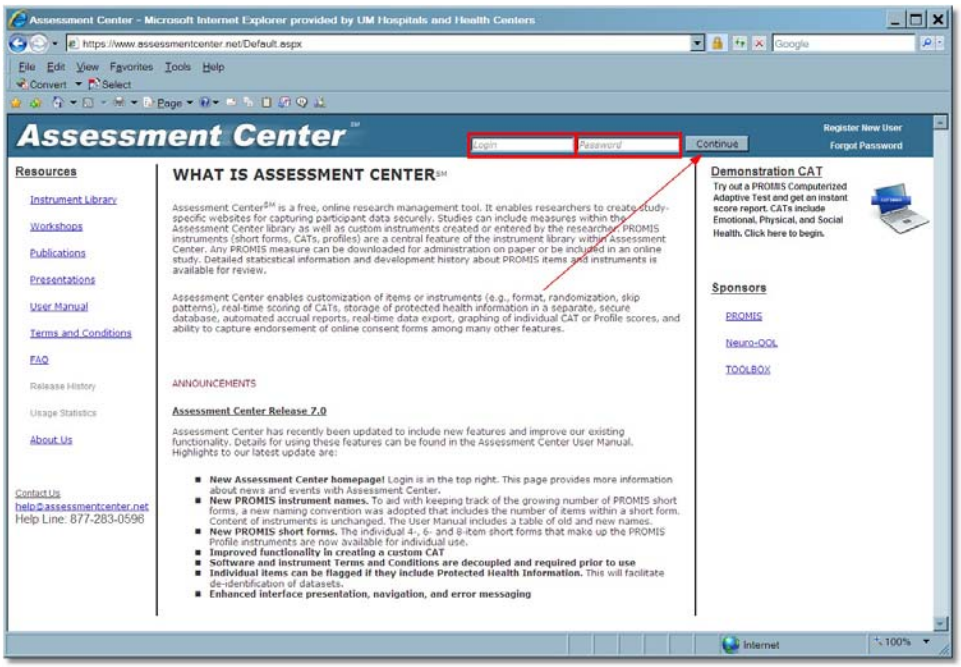
Your registration is now complete. Email Ellen Woodard (erhw@umich.edu) to let her know you've completed your registration so she can add you to the NEPTUNE study team. Once you are added to the NEPTUNE study team you will be able to register study participants (refer to PROMIS_PRegistration.pdf) so they can access and complete the PROMIS survey.

PROMIS Assessment Center

Participant Registration

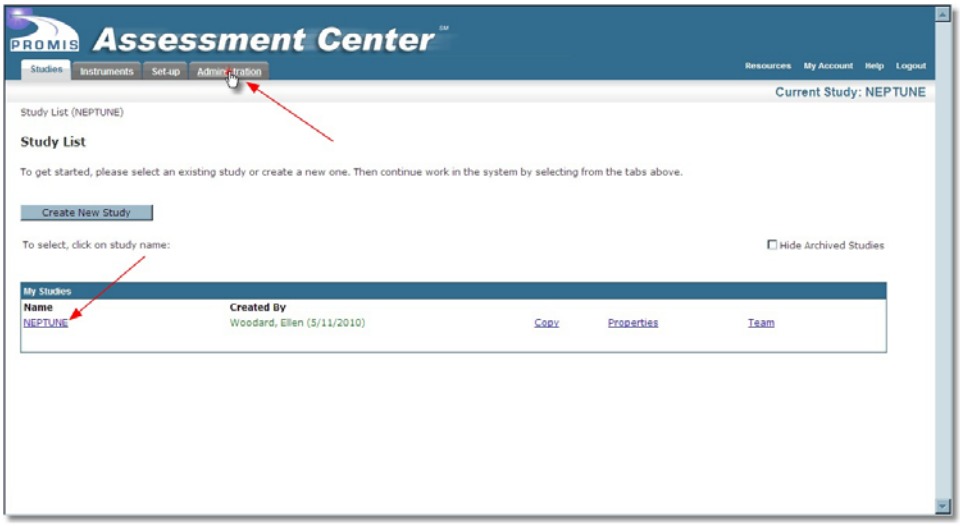
NOTE: You must complete the ***Study Coordinator Registration*** (refer to PROMIS_SCRegistration.pdf) and have notified Ellen Woodard (erhw@umich.edu) that you completed that registration before you can register participants.

1. Go to the Assessment Center web page – www.assessmentcenter.net/ac1 - and enter the User ID and password you supplied upon ***Study Coordinator Registration***, then click the "Continue" button.

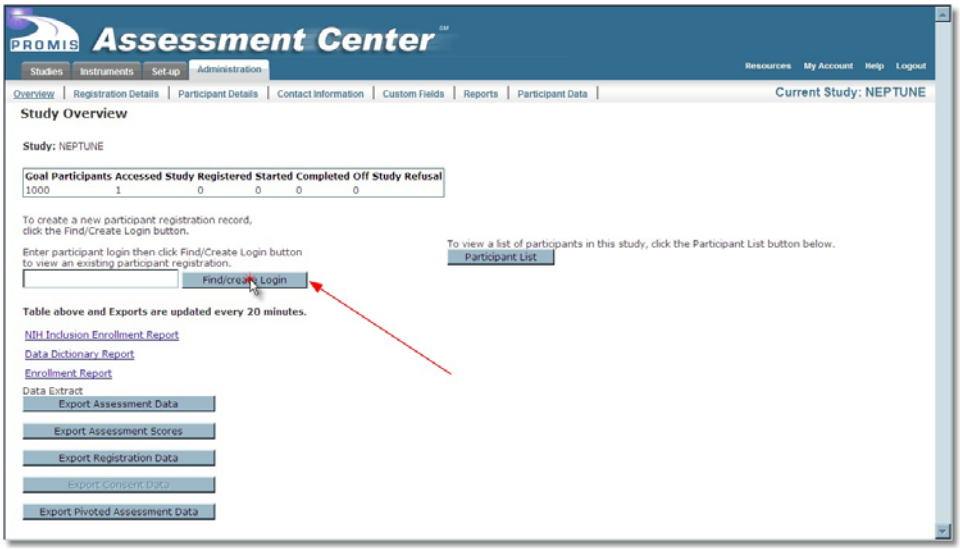


   If you forget your password, click on the "Forgot Password" link and the Assessment Center will automatically email your password to the email address you supplied upon registration.

2. Click on the "Administration" tab. NOTE: You may first need to "select" the study by clicking on "NEPTUNE" in the "Name" column of the "My Studies" list.



3. Click the "Find/Create Login" button.



4. Complete all of the following fields (any field not mentioned is to be left as is):

   a. <u>Registration Details tab</u>

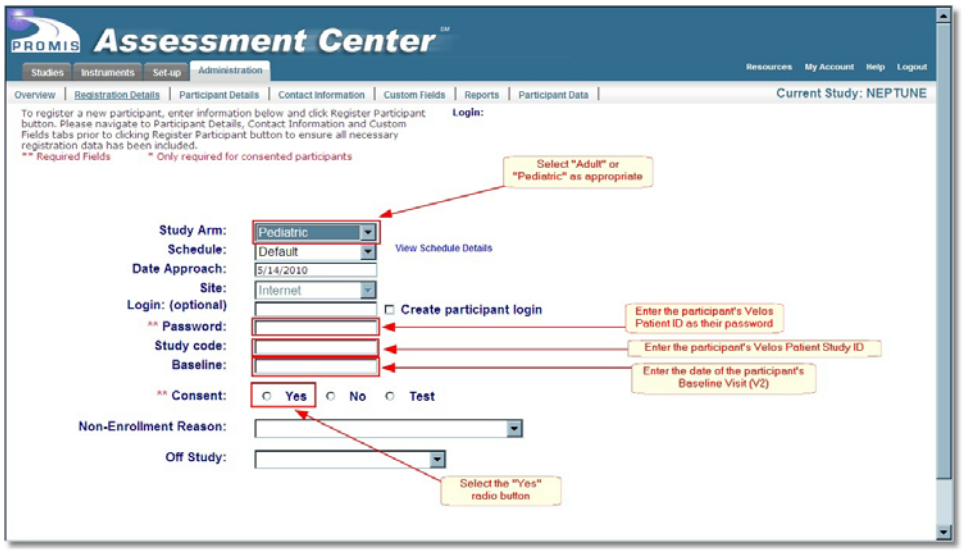
      (1) Study Arm – select "Adult" or "Pediatric" as appropriate

      (2) Password – enter the participant's ***Velos Patient ID*** as their password

      (3) Study code – enter the participant's ***Velos Patient Study ID***

      (4) Baseline – enter the date of the participant's Baseline Visit (V2)

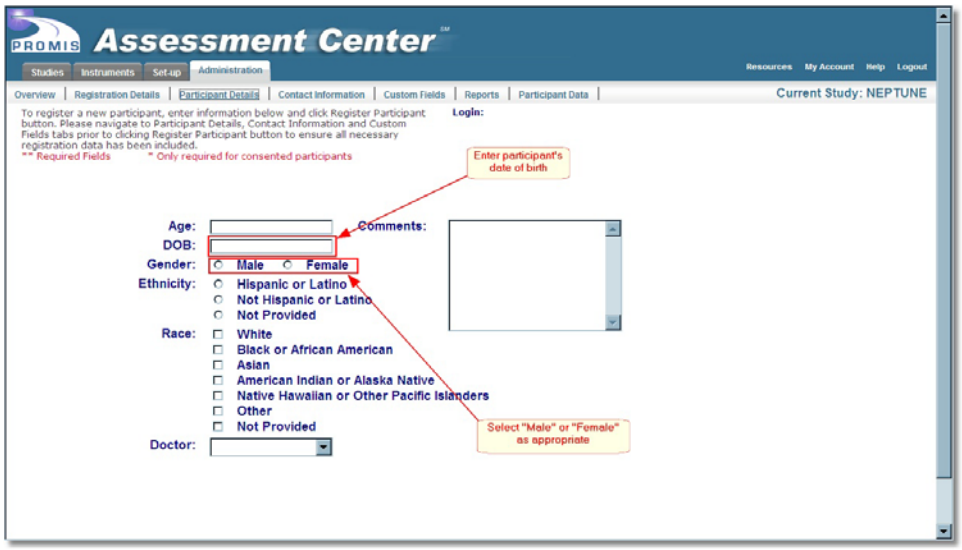
      (5) Consent – select the "Yes" radio button



b. <u>Participant Details tab</u>

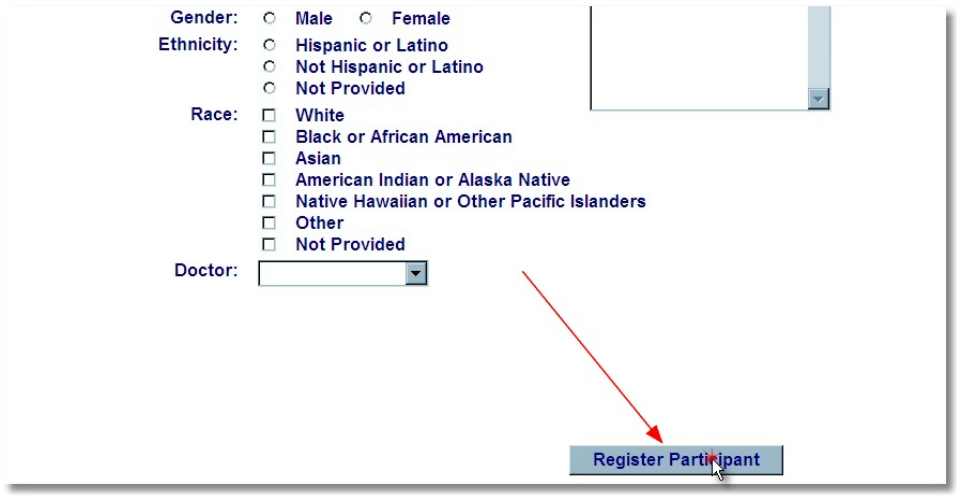
(1) DOB – enter the participant's date of birth

(2) Gender – select "Male" or "Female" as appropriate

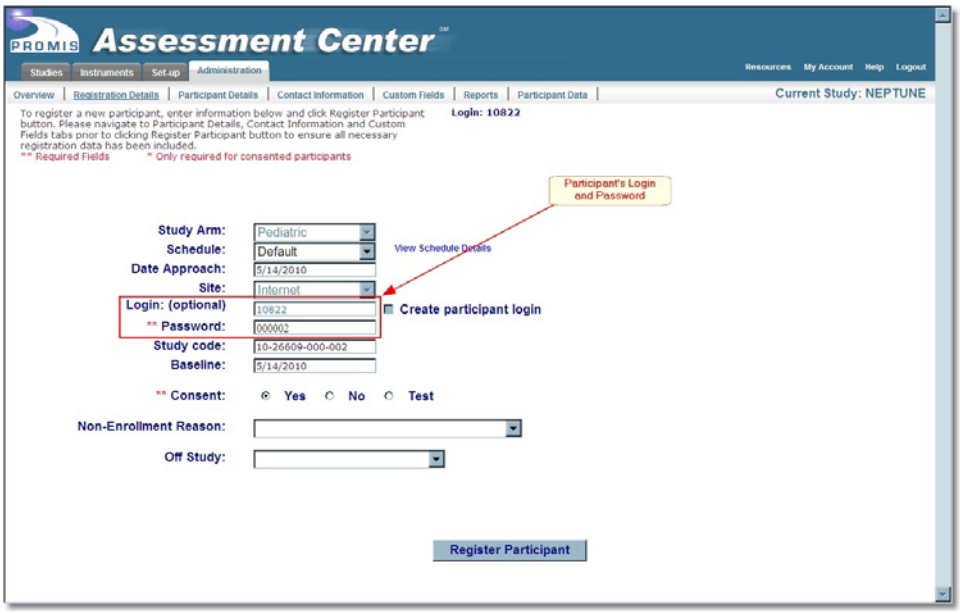


Again, the above-mentioned fields are the only ones that need to be completed. Any field not mentioned is to be left as is.

5. Click the "Register Participant" button.



6. Make note of the participant's assigned Login and password.



7. Click "Logout" (upper right-hand corner of the page) to exit the Assessment Center

You can now provide your participant with their assigned Login and password and they can log in to take the survey at www.assessmentcenter.net/ac1/assessments/NEPTUNE

21. Appendix H. Medical Diary

The medication diary/tracker should be provided to participants at their first consented study contact. As necessary, create additional copies of the first page, and instruct the participant about completing the actual log on the following page.

If participants were not provided the medical diary/tracker at their first consented study contact, it can be provided at any time throughout the duration of the study. Participants should be encouraged to complete these forms completely, and be an active participant in their health care monitoring. Additional sheets can be provided as necessary.

Nephrotic Syndrome Study Network

Medication Tracker

It is very important that you take your medications every day, exactly as your doctor(s) prescribed. This medication tracker has two parts; the first part lists all your medication and how they should be taken (make copies for additional meds as necessary). The second part is a medication diary for you to keep track of your medications and any changes between NEPTUNE study visits.

If you need help completing this form, your research coordinator can help you complete it. Please keep this form updated whenever your medications change (even if it is just a dosage change) and bring this with you to all study visits.

My Medications:

Medication name:
Dosage (strength of pills): **I take:** *pills, at* *am/pm*
What the medicine does:
I take it: *time per day* **With:**
If I miss a dose, I should:
The doctor also said:

Medication name:
Dosage (strength of pills): **I take:** *pills, at* *am/pm*
What the medicine does:
I take it: *time per day* **With:**
If I miss a dose, I should:
The doctor also said:

Medication name:
Dosage (strength of pills): **I take:** *pills, at* *am/pm*
What the medicine does:
I take it: *time per day* **With:**
If I miss a dose, I should:
The doctor also said:

Medication name:
Dosage (strength of pills): **I take:** *pills, at* *am/pm*
What the medicine does:
I take it: *time per day* **With:**
If I miss a dose, I should:
The doctor also said:

Study Medication Tracker

Medication Name	Dose (1 tab, 20 mg)	Frequency (how often?)	How taken: (oral, inhalant)	Date Started	Date Stopped

22. Appendix I. Birth History

Pictured below is the inside of birth history tri-fold hand out, to be provided by NEPTUNE DACC to all sites. It can also be printed locally if quality color printing is available. Research Coordinators should instruct participants to take this pamphlet home with them and inquire with family about their birth history if it is unknown to them, as well as their primary and secondary caregiver's educational history and biological parents' age and race.

This document should have been submitted as part of the Protocol V3.0 Amendment. If this was not IRB approved, please obtain proper approval prior to use.

neptune **Participant Birth History**

The details of your birth history might provide NEPTUNE investigators new insights into risk factors for your kidney disease. If you are a woman, details of your pregnancies may also provide more understanding of the course of your kidney disease.

Looking back to knowingly look ahead...

Parental Socio-demographics

My mother (or primary caregiver/guardian) completed schooling through:

_____ Grade _____ High school diploma or equivalent
_____ 2 year associates degree/certificate
_____ 4 year college degree
_____ Master's level diploma
_____ Graduate level diploma (MD, PhD, PharmD, etc)
_____ Don't know _____ Not applicable

My biological mother's age when I was born: _____years

My biological mother's race (check all that apply):

____American Indian/Alaskan Native
____Black/African American
____Native Hawaiian/Other Pac Islander
____Unknown
____Asian/Asian American
____Hispanic/Latina
____White/Caucasian
____Other (please specify):

_____

My father (or secondary caregiver/guardian) completed schooling through:

_____ Grade _____ High school diploma or equivalent
_____ 2 year associates degree/certificate
_____ 4 year college degree
_____ Master's level diploma
_____ Graduate level diploma (MD, PhD, PharmD, etc)
_____ Don't know _____ Not applicable

My biological father's age when I was born: _____years

My biological father's race (check all that apply):

____American Indian/Alaskan Native
____Black/African American
____Native Hawaiian/Other Pac Islander
____Unknown
____Asian/Asian American
____Hispanic/Latina
____White/Caucasian
____Other (please specify):

_____

My Birth History

The following details are about the NEPTUNE study participant

Birth weight: _____ lbs._____oz.
or _____ grams

Birth length: _____inches/centimeters (circle one)

I was born in a hospital: ( ) Yes ( ) No
( ) Don't know

I was delivered: ( ) Vaginally ( ) C-section
( ) Don't know

I was: ( ) Full term ( ) Don't know
( ) Premature: _____ # weeks
( ) Don't know

I was part of a multiple birth (twins, triplets, etc):
( ) Yes ( ) No ( ) Don't know

Immediately after I was born I was in the neo-natal intensive care unit or ICU: ( ) Yes ( ) No
( ) Don't know

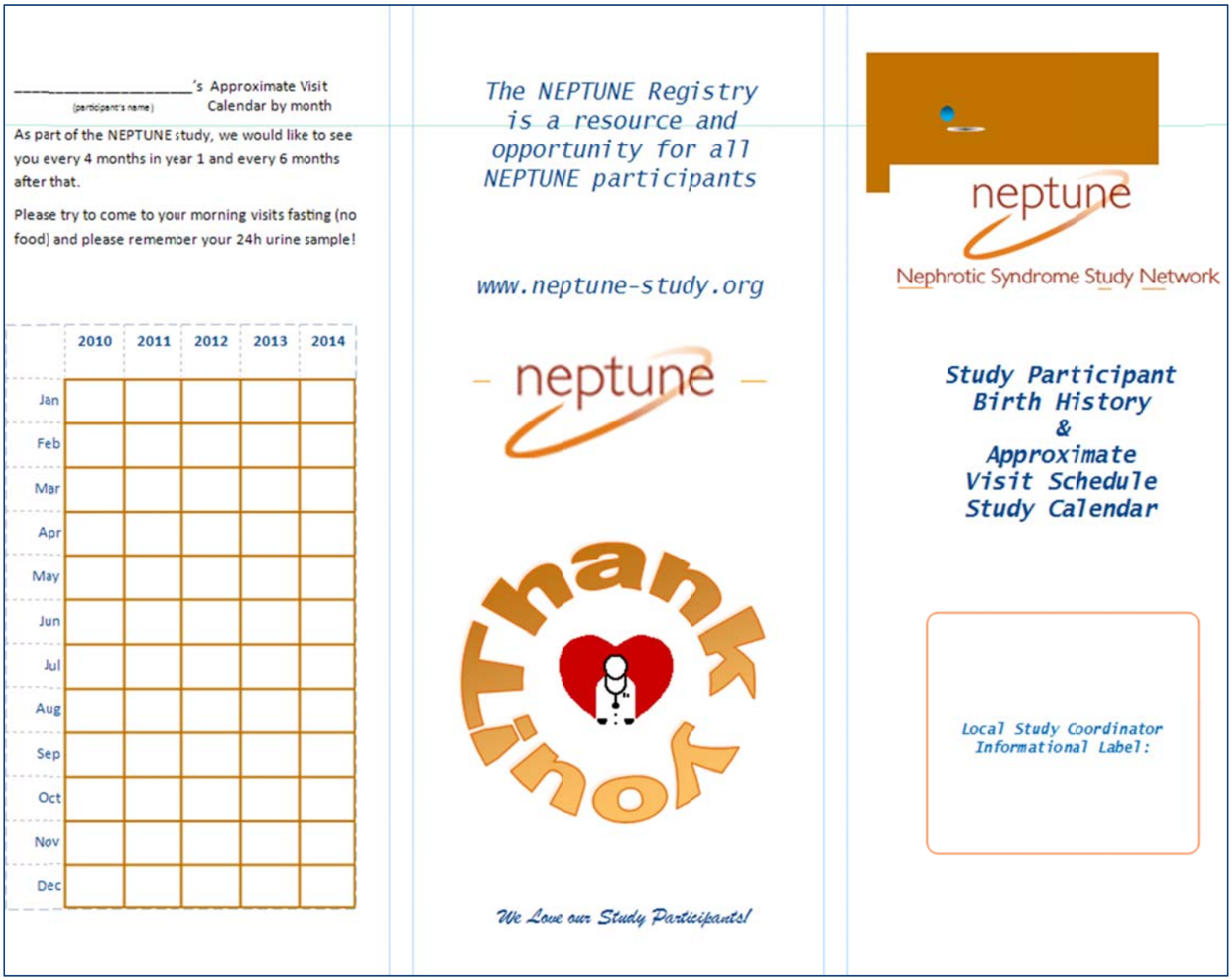
Immediately after I was born, I had kidney problems:
( ) Yes ( ) No ( ) Don't know

Time I spent in the hospital after I was born:
( ) Days ( ) Don't know ( ) Not applicable

The Nephrotic Syndrome Study Network is funded through:

The National Institutes of Health
The National Institute for Diabetes, Digestive and Kidney Diseases
The Office of Rare Diseases Research
The NephCure Foundation
The University of Michigan

Outside of Tri-fold hand out. The site Research Coordinator should complete the approximate visit schedule for their participants, and remind them that the study is longitudinal and we hope to follow them for the duration of the study.



_____'s Approximate Visit Calendar by month
(participant's name)

As part of the NEPTUNE study, we would like to see you every 4 months in year 1 and every 6 months after that.

Please try to come to your morning visits fasting (no food) and please remember your 24h urine sample!

	2010	2011	2012	2013	2014
Jan					
Feb					
Mar					
Apr					
May					
Jun					
Jul					
Aug					
Sep					
Oct					
Nov					
Dec					

The NEPTUNE Registry is a resource and opportunity for all NEPTUNE participants

www.neptune-study.org

neptune

Thank You!

We Love our Study Participants!

neptune

Nephrotic Syndrome Study Network

Study Participant Birth History & Approximate Visit Schedule Study Calendar

Local Study Coordinator Informational Label:

23. Appendix J. Blood Collection Protocol

23.A. Baseline Biospecimen Collection

The data and specimens obtained at the Baseline Visit [V2] will serve as the baseline study data for the purpose of data analysis and biochemical investigations. The Baseline Visit will include the following biospecimens procurement.

23.A.1. Blood Specimens

Fasting blood draw (Adult max: 115 cc, pediatrics by weight according to table below) for the NEPTUNE Biorepository and central biochemical laboratory samples including lipid profile, glucose, total cholesterol and triglycerides. Blood volumes will be reduced in pediatric participants and in all participants, adult and pediatric, with a hematocrit below 28%. If the baseline visit occurs on the same day as biopsy visit [V3], the blood draw will be deferred to a subsequent day, but not later than 30 days after the procedure.

Adults (age 18+):

Visit	Blood Draw Volume
Baseline [V2]	**115 mL**
Biopsy [V3]	10 mL
Follow-up [V4-13]	65 mL

Children as follows by weight:

Visit	Blood Draw Volume by Weight (in pounds)		
	< 21 pounds	21-51 pounds	≥ 52 pounds
Baseline [V2]	**20 cc**	**50 cc**	**100 cc**
Biopsy [V3]	10 cc	10 cc	10 cc
Follow-up [V4-13]	20 cc	50 cc	65 cc

Adult participants with a clinically reported hematocrit < 28%; the blood draw should be reduced to the >52 pound children draw at baseline; and 21-51 pound draw at follow-up.

Pediatric participants should be reduced to the next lower weight group; children < 20 pounds will not undergo a blood draw at a visit in which a clinically reported hematocrit < 28% within 30 days of study visit.

Local site phlebotomy practice should be used. Research samples will not be submitted for any clinical measures, so please coordinate with treating physicians if they are in need of standard of care blood draws.

23.A.2. Blood Specimens Order of precedence

The blood draw order should follow the number identified on each tube from smallest to largest (in the case of pediatric draws based on weight).

Local phlebotomy practice should be followed for blood draw attempts and institutional policy should be observed for number of attempts to obtain the research blood draw.

If a participant blood draw is suboptimal (a “difficult stick” or perfusion is weak) please immediately prioritize the tube order to a minimum of one EDTA tube (tubes 6-9 for adults and pediatrics >52 pounds, 14-15 for pediatrics <52 pounds) and the RNA Paxgene tube (Tube 12).

The following table is meant as a guide for order of tube draw when a full blood sample is optimal. Please observe the corresponding weight for pediatric participants.

Adult participant baseline visit draw order:

Tube #	Tube Type	Baseline Visit [V2]
1	4.5 mL Sodium Citrate	**4.5**
2	10 mL Serum wrapped in foil	**10**
16	3 mL Serum wrapped in Foil	
3	10 mL SST	**10**
4	10 mL SST wrapped in foil	**10**
17	3.5 mL SST wrapped in foil	
5	4 mL Sodium Heparin in Foil	**4**
18	2 mL Sodium Heparin in Foil	
6	10 mL EDTA	**10**
7	10 mL EDTA	**10**
8	10 mL EDTA	**10**
9	10 mL EDTA	**10**
10	10 mL EDTA	**10**
11	10 mL EDTA - Iced	**10**
14	4 ml EDTA	
15	6 mL EDTA	
12	2.5 mL RNA	**2.5**
13	8.5 mL DNA	**8.5**
Blood Draw Totals:		**109.5**

Pediatric participant baseline visit draw order by weight:

Tube #	Tube Type	< 21 pounds	21-51 pounds	≥ 52 pounds
		Baseline [V2]	**Baseline [V2]**	**Baseline [V2]**
1	4.5 mL Sodium Citrate		**4.5**	**4.5**
2	10 mL Serum wrapped in foil		**10**	**10**
16	3 mL Serum wrapped in Foil	**3**		
3	10 mL SST			**10**
4	10 mL SST wrapped in foil		**10**	**10**
17	3.5 mL SST wrapped in foil	**3.5**		
5	4 mL Sodium Heparin in Foil		**4**	**4**
18	2 mL Sodium Heparin in Foil	**2**		
6	10 mL EDTA		**10**	**10**
7	10 mL EDTA*			**10**

Tube #	(cont'd) Tube Type	< 21 pounds	21-51 pounds	≥ 52 pounds
		Baseline [V2]	**Baseline [V2]**	**Baseline [V2]**
8	10 mL EDTA			**10**
9	10 mL EDTA			**10**
14	4 ml EDTA (ICED except <21)	**4**	**4**	**4**
15	6 mL EDTA*	**5**	**5**	**6**
12	2.5 mL RNA	**2.5**	**2.5**	**2.5**
13	8.5 mL DNA		**0**	**8.5**
Blood Draw Totals:		**20**	**50**	**99.5**

*The DNA tube should only be obtained one time over the course of the study. Once the DNA draw is complete, for subsequent visits please supplement the 8.5 mL DNA draw with a complete 10 mL EDTA tube draw. (This applies for 21-51 pound participant follow-up visits).

23.B. V3 Biopsy Visit Biospecimen Collection

The data and specimens obtained at the V3 Biopsy Visit has been added to the study procedures effective Protocol V3.0 at each site. This data will serve as the baseline study data for the purpose of data analysis and biochemical investigations for participants who do not return to study sites for follow-up. The Baseline Visit should still be pursued for all consented participants.

23.B.1. Blood Specimens

Fasting blood draw (Adult and pediatric max: 10 cc) for the NEPTUNE Biorepository and central biochemical laboratory samples including lipid profile, glucose, total cholesterol and triglycerides. If the baseline visit occurs on the same day as biopsy visit [V3], the Baseline Visit [V2] blood draw will be deferred to a subsequent day, but not later than 30 days after the procedure; however, the V3 Biospecimen 10 cc blood draw should be obtained.

Adults (age 18+):

Visit	Blood Draw Volume
Baseline [V2]	**115 mL**
Biopsy [V3]	**10 mL**
Follow-up [V4-13]	65 mL

Children as follows by weight:

Visit	Blood Draw Volume by Weight (in pounds)		
	< 21 pounds	21-52 pounds	≥ 52 pounds
Baseline [V2]	**20 cc**	**50 cc**	**100 cc**
Biopsy [V3]	**10 cc**	**10 cc**	**10 cc**
Follow-up [V4-13]	20 cc	50 cc	65 cc

Local site phlebotomy practice should be used. Research samples will not be submitted for any clinical measures, so please coordinate with treating physicians if they are in need of standard of care blood draws.

There is no order of prioritization for V3 blood draw. Please obtain all 3 tubes indicated here:

Tube #	Tube Type	Biopsy Visit [V3]
19	3 mL SST	**3**
14	4 ml EDTA	**4**
12	2.5 mL RNA	**2.5**
Blood Draw Totals:		**9.5**

23.C. Follow-up Biospecimen Collection

The data and specimens obtained at the Follow-up Visits [V4-13] will serve as ongoing study data for the longitudinal purpose of data analysis and biochemical investigations. The Follow-up Visits will include a subset of the baseline biospecimens procurement.

23.C.1. Blood Specimens

Fasting blood draw (Adult max: 115 cc, pediatrics by weight according to table below) for the NEPTUNE Biorepository and central biochemical laboratory samples including lipid profile, glucose, total cholesterol and triglycerides. Blood volumes will be reduced in pediatric participants and in all participants, adult and pediatric, with a hematocrit below 28%. If the baseline visit occurs on the same day as biopsy visit [V3], the blood draw will be deferred to a subsequent day, but not later than 30 days after the procedure.

Adults (age 18+):

Visit	Blood Draw Volume
Baseline [V2]	115 mL
Biopsy [V3]	10 mL
Follow-up [V4-13]	**65 mL**

Children as follows by weight:

Visit	Blood Draw Volume by Weight (in pounds)		
	< 21 pounds	21-52 pounds	≥ 52 pounds
Baseline [V2]	20 cc	50 cc	100 cc
Biopsy [V3]	10 cc	10 cc	10 cc
Follow-up [V4-13]	**20 cc**	**50 cc**	**65 cc**

Adult participants with a clinically reported hematocrit < 28%; the blood draw should be reduced to the >52 pound children draw at baseline; and 21-51 pound draw at follow-up.

Pediatric participants should be reduced to the next lower weight group; children < 20 pounds will not undergo a blood draw at a visit in which a clinically reported hematocrit < 28% within 30 days of study visit.

Local site phlebotomy practice should be used. Research samples will not be submitted for any clinical measures, so please coordinate with treating physicians if they are in need of standard of care blood draws.

Adult participant follow-up visit draw order:

Tube #	Tube Type	Follow-up Visits [V4-V13]
1	4.5 mL Sodium Citrate	**4.5**
2	10 mL Serum wrapped in foil	
16	3 mL Serum wrapped in Foil	**3**
3	10 mL SST	**10**
4	10 mL SST wrapped in foil	
17	3.5 mL SST wrapped in foil	**3.5**
5	4 mL Sodium Heparin in Foil	
18	2 mL Sodium Heparin in Foil	**2**
6	10 mL EDTA	**10**
7	10 mL EDTA	**10**
8	10 mL EDTA	**10**
9	10 mL EDTA- Iced	**10**
10	10 mL EDTA	
11	10 mL EDTA	
14	4 ml EDTA	
15	6 mL EDTA	
12	2.5 mL RNA	**2.5**
13	8.5 mL DNA	
Blood Draw Totals:		**65.5**

Pediatric participant follow-up visit draw order by weight:

Tube #	Tube Type	< 21 pounds	21-51 pounds	> 52 pounds
		Follow-up [V4-13]	**Follow-up [V4-13]**	**Follow-up [V4-13]**
1	4.5 mL Sodium Citrate		**4.5**	**4.5**
2	10 mL Serum wrapped in foil		**10**	**10**
16	3 mL Serum wrapped in Foil	**3**		
3	10 mL SST			**10**
4	10 mL SST wrapped in foil		**10**	**10**
17	3.5 mL SST wrapped in foil	**3.5**		
5	4 mL Sodium Heparin in Foil		**4**	**4**
18	2 mL Sodium Heparin in Foil	**2**		
6	10 mL EDTA		**10**	**10**
7	10 mL EDTA			**10**

Tube #	(cont'd) Tube Type	< 21 pounds	21-51 pounds	≥ 52 pounds
		Follow-up [V4-13]	Follow-up [V4-13]	Follow-up [V2]
8	10 mL EDTA			
9	10 mL EDTA			
14	4 ml EDTA (ICED except <21)	**4**	**4**	**4**
15	6 mL EDTA*	**5**	**5**	
12	2.5 mL RNA	**2.5**	**2.5**	**2.5**
13	8.5 mL DNA		**8.5**	**0**
Blood Draw Totals:		**20**	**50***	**65**

*The DNA tube should only be obtained one time over the course of the study. Once the DNA draw is complete, for subsequent visits please supplement the 8.5 mL DNA draw with a complete 10 mL EDTA tube draw. (This applies for 21-51 pound participant follow-up visits).

24. Appendix K. Urine Collection Protocol

In an effort to best accommodate study participants 24-hour collections will be coordinated as necessary with local clinical needs. Determine if the treating physician is requesting a 24-hour urine collection.

If yes:

- Follow your local site's protocol 24-hour urine collection
- Request the study participant to bring their sample to the research visit first.
- Pour off the requested aliquot (see 24-hour MOP); write legibly on the specimen container the volume removed.
- Provide a weight if necessary

If no clinical 24-hour urine collection is necessary, provide the participant a printed copy of the instructions at the end of this appendix, along with the urine collection materials.

Per Protocol V2.5, effective 4/2010 study participants are to be compensated $50.00 for each successful 24-hour urine collection to offset the inconvenience of this necessary study procedure.

24.A. Baseline Urine Collections

The baseline urine collections are necessary components for the primary outcomes of the study. As the current "gold standard" for protein and creatinine measurements, it is essential that the collections are done properly. If for research purposes only, please review the urine collection materials at the end of this appendix with your study participant, providing specimen collection materials including large, unmarked gallon jug and cap, and either a urinal (males) or a urine hat (females and young pediatric participants). These items can be provided by the NEPTUNE Biorepository via the Kit Request Form (See 16. Appendix C).

24.A.1. 24-hour Urine Collection

The 24-hour urine collection is critical for the baseline visit. As the current "gold standard" for protein and creatinine measurements, it is essential that the collection is done properly. If for research purposes only, please review the urine collection materials at the end of this appendix with your study participant, providing specimen collection materials including large, unmarked gallon jug and cap, and either a urinal (males) or a urine hat (females and young pediatric participants). These items can be provided by the NEPTUNE Biorepository via the Kit Request Form (See 16. Appendix C).

24.A.2. Timed Urine Collection

In an effort to best accommodate study participants, timed urine collections and capture will be coordinated as necessary with local clinical needs for children below five years of age and other incontinent participants. Determine if the treating physician is requesting a timed urine collection for the study participant.

Please follow your local site's standard protocol for timed urine collection and urine capture.

The instructions on the last page can be modified to record the necessary details for both a timed urine collection or urine capture.

24.A.3. Baseline Random/Spot Clean Catch Urine Collection

A "clean catch" research urine sample will be collected from all participants. Approximately 60 cc of the "clean catch" urine will be processed and transferred to the NEPTUNE Biorepository.

When the study participant is able, during the course of the study visit, provide a specimen cup.

Using the local site's clean catch protocol, obtain a specimen for processing immediately following the study visit.

A "clean catch" sample may also be known locally as a "spot collection" or "fresh urine". Please be sure to instruct your participants on the necessary procedure for "clean catch" samples.

24.B. Biopsy Random/Spot Clean Catch Urine Collection

A "clean catch" research urine sample will be collected from all participants prior to biopsy. This sample may be obtained up to 7 days prior to biopsy procedure or 7 days post-biopsy. The preferred timing is day of biopsy, prior to procedure. "clean catch" urine samples cannot be obtained post-biopsy for 3 days.

Approximately 60 cc of the "clean catch" urine will be processed and transferred to the NEPTUNE Biorepository.

Using the local site's clean catch protocol, obtain a specimen for processing immediately following the study visit.

A "clean catch" sample may also be known locally as a "spot collection" or "fresh urine". Please be sure to instruct your participants on the necessary procedure for "clean catch" samples.

24.C. Follow-up Urine Collections

The 24-hour urine collection is critical at annual visits. When possible, please obtain a 24-hour urine at every visit, with a minimum collection annually. Determine if the 24-hour urine is necessary for clinical purposes or just research purposes and proceed as described for the baseline 24-hour urine collection. Timed collections are also acceptable as indicated above.

A "clean catch" research urine sample will be collected from all participants at all follow-up visits. Please review the above procedures for each urine type collection.

24.D. 24-Hour Urine Collection Instructions

Dear _____:

Instructions for your 24-hour urine collection

1. **You will be given a 24-hour urine collection bottle. It will need to be kept in the refrigerator or on ice.**

2. **Always start your 24-hour urine collection in the morning once you begin your collection of urine.**

3. **Do not save the first urine of the day, but mark this as your START TIME at the bottom of this sheet.**

4. **Save all urine for the next 24 hours in the collection bottle. In order to get correct results, it is important to save every urine sample. If you forget to save any urine, please report to your NEPTUNE Coordinator:**

   _____
   (please print your name)

   You will need to drink plenty of fluids during this time, 6-8 (8 oz.) glasses if possible.

5. **The last urine sample should be as close to the starting time as possible and must be saved.**

6. **Please remember to keep urine in collection bottle in refrigerator or on ice.**

Bring bottle(s) to: _____
(Study Visit Location)

Please complete the following information:

Patient Name:_____

Collection Start Date:_____ **Start Time:**_____**am/pm**

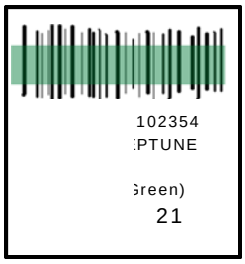
Collection Stop Date:_____ **Stop Time:**_____**am/pm**

Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]** BIOPSY TISSUE

Procedure Overview
This procedure describes the process for storing renal biopsy tissue for the NEPTUNE Biobank at -80° C. Shipping details are provided in 27. Appendix N Shipping.

Required Supplies:
Included in kit:

- 1 pre-labeled cryovial[1] containing 1.6 mL RNA-Later[2]



Provided by site:

- Renal tissue sample from study participant
- Gloves, goggles, and lab coat

Required Equipment:

- No equipment is necessary for this specimen

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, Site PI or designated individual would serve as alternates.

Only a nephrologist or other trained healthcare professional is able to do the renal biopsy.

Procedure
The green-labeled, green-capped cryovial containing RNA-Later MUST be present during the biopsy procedure. Specimen must be placed directly into RNA-later and not be immersed in other fixative solutions prior to storage.

1. Attending physician will procure the renal tissue core during procedure
2. In sterile fashion, the attending physician will procure one full core from specimens obtained
3. In sterile fashion, place the specimen in the green-labeled, green capped cryovial and place lid on, rotating cap to the right to close completely.
4. The specimen in RNA-Later solution is stable at room temperature until return to lab.

Shipping:
Biopsy specimens should be stored with the respective NEPTUNE Participant samples. If Baseline [V2] has not yet occurred, please take care in storing the single cryovial in a -80 freezer. Samples should be shipped with the respective kit.

All specimens should be shipped together **on dry ice** using the NEPTUNE shipping vendor and container provided by the NEPTUNE DACC/Biobank.

Documentation
All corresponding samples for each participant number should be stored together. Please note, effective 6/2012 the number of passes to obtain the research core must be documented in Kidney Specimens Worksheet 11A and documented in the corresponding CRF.

References
1. Cryovials: DOT Scientific Inc. No. T334-6SPR
2. See attached MSDS

Relevant Definitions
None

Applied Biosystems

Ambion®
THE RNA COMPANY®
An Applied Biosystems Business

MSDS PART NUMBER: 4381859 US
OHS PART NUMBER: 00232284
Revision number : A

MATERIAL SAFETY DATA SHEET

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

AMBION, INC
2130 WOODWARD ST.
AUSTIN, TX 78744
(512) 651-0200 (USA)
EMERGENCY CONTACT:
1-800-424-9300 (NORTH AMERICA)
WEB ADDRESS: www.ambion.com
MAIL: techserv@ambion.com

AMBION, INC
LTD HUNTINGDON
CAMBIDGESHIRE, UK PE29 6XY
+44 1480 373 020 (UK)
EMERGENCY CONTACT:
+1-703-527-3887, REVERSE CHARGES (INTERNATIONAL)
MAIL: eurotech@ambion.com

SUBSTANCE: RNAlater®

TRADE NAMES/SYNONYMS:
US MSDS P/N 4381859; P/N AM7020; P/N AM7021; P/N AM7022; P/N AM7023; P/N AM7024; P/N SAM7023; P/N 7020; P/N 7021; P/N 7022; P/N 7023; P/N 7024; P/N 7020G; P/N 7022G1; 00232284

PRODUCT USE: For Research Use Only. Not for use in diagnostic procedures.

CREATION DATE: Nov 13 2006
REVISION DATE: Jan 08 2007

2. COMPOSITION, INFORMATION ON INGREDIENTS

COMPONENT: TRADE SECRET 00232384
CAS NUMBER: Not assigned.
PERCENTAGE: 30-60

COMPONENT: TRADE SECRET 00232322
CAS NUMBER: Not assigned.
PERCENTAGE: <10

COMPONENT: SULFURIC ACID
CAS NUMBER: 7664-93-9

PERCENTAGE: <0.1

3. HAZARDS IDENTIFICATION

NFPA RATINGS (SCALE 0-4): HEALTH=2 FIRE=1 REACTIVITY=0

EMERGENCY OVERVIEW:
PHYSICAL FORM: solution
MAJOR HEALTH HAZARDS: respiratory tract irritation, skin irritation, eye irritation

POTENTIAL HEALTH EFFECTS:
INHALATION:
SHORT TERM EXPOSURE: irritation, cough, sore throat, difficulty breathing, lung congestion
LONG TERM EXPOSURE: irritation
SKIN CONTACT:
SHORT TERM EXPOSURE: irritation
LONG TERM EXPOSURE: irritation
EYE CONTACT:
SHORT TERM EXPOSURE: irritation
LONG TERM EXPOSURE: irritation
INGESTION:
SHORT TERM EXPOSURE: irritation, sore throat, nausea, vomiting, diarrhea, stomach pain, convulsions
LONG TERM EXPOSURE: no information on significant adverse effects

4. FIRST AID MEASURES

INHALATION: If adverse effects occur, remove to uncontaminated area. Give artificial respiration if not breathing. Get immediate medical attention.

SKIN CONTACT: Wash skin with soap and water for at least 15 minutes while removing contaminated clothing and shoes. Get medical attention, if needed. Thoroughly clean and dry contaminated clothing and shoes before reuse.

EYE CONTACT: Flush eyes with plenty of water for at least 15 minutes. Then get immediate medical attention.

INGESTION: If a large amount is swallowed, get medical attention.

5. FIRE FIGHTING MEASURES

FIRE AND EXPLOSION HAZARDS: Slight fire hazard.

EXTINGUISHING MEDIA: carbon dioxide, regular dry chemical, regular foam, water

FIRE FIGHTING: Move container from fire area if it can be done without risk. Avoid inhalation of material or combustion by-products. Stay upwind and keep out of low areas.

FLASH POINT: No data available.

HAZARDOUS COMBUSTION PRODUCTS:
Thermal decomposition products or combustion: oxides of carbon, oxides of nitrogen

6. ACCIDENTAL RELEASE MEASURES

WATER RELEASE:
Subject to California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65). Keep out of water supplies and sewers.

OCCUPATIONAL RELEASE:
Stop leak if possible without personal risk. Small spills: Absorb with sand or other non-combustible material. Collect spilled material in appropriate container for disposal. Notify Local Emergency Planning Committee and State Emergency Response Commission for release greater than or equal to RQ (U.S. SARA Section 304). If release occurs in the U.S. and is reportable under CERCLA Section 103, notify the National Response Center at (800)424-8802 (USA) or (202)426-2675 (USA).

7. HANDLING AND STORAGE

STORAGE: Store and handle in accordance with all current regulations and standards. See original container for storage recommendations. Keep separated from incompatible substances.

8. EXPOSURE CONTROLS, PERSONAL PROTECTION

EXPOSURE LIMITS:
RNAlater®:
No occupational exposure limits established.

VENTILATION: Provide local exhaust ventilation system. Ensure compliance with applicable exposure limits.

EYE PROTECTION: Wear splash resistant safety goggles with a faceshield. Provide an emergency eye wash fountain and quick drench shower in the immediate work area.

CLOTHING: Wear appropriate chemical resistant clothing.

GLOVES: Wear appropriate chemical resistant gloves.

RESPIRATOR: Under conditions of frequent use or heavy exposure, respiratory protection may be needed. Respiratory protection is ranked in order from minimum to maximum. Consider warning properties before use.
Any chemical cartridge respirator with organic vapor cartridge(s).
Any chemical cartridge respirator with a full facepiece and organic vapor cartridge(s).
Any air-purifying respirator with a full facepiece and an organic vapor canister.
For Unknown Concentrations or Immediately Dangerous to Life or Health -
Any supplied-air respirator with full facepiece and operated in a pressure-demand or other positive-pressure mode in combination with a separate escape supply.
Any self-contained breathing apparatus with a full facepiece.

9. PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL STATE: liquid
APPEARANCE: clear
PHYSICAL FORM: solution
ODOR: Not available
BOILING POINT: Not available
FREEZING POINT: Not available
VAPOR PRESSURE: Not available
VAPOR DENSITY: Not available
SPECIFIC GRAVITY: Not available
WATER SOLUBILITY: miscible
PH: 4.5
VOLATILITY: Not available
ODOR THRESHOLD: Not available
EVAPORATION RATE: Not available
COEFFICIENT OF WATER/OIL DISTRIBUTION: Not available

10. STABILITY AND REACTIVITY

REACTIVITY: Stable at normal temperatures and pressure.

CONDITIONS TO AVOID: Avoid heat, flames, sparks and other sources of ignition.
Avoid contact with incompatible materials.

INCOMPATIBILITIES: acids, bases, chlorates, chlorine, copper alloys, copper, hypochlorite, nitrates, nitrite salts, oxidizing materials, potassium compounds, zinc

HAZARDOUS DECOMPOSITION:
Thermal decomposition products or combustion: oxides of carbon, oxides of nitrogen

POLYMERIZATION: Will not polymerize.

11. TOXICOLOGICAL INFORMATION

TRADE SECRET 00232384:
IRRITATION DATA: 50 percent/5 day(s)-intermittent skin-mammal
TOXICITY DATA: 2840 mg/kg oral-rat LD50
LOCAL EFFECTS:
Irritant: inhalation, skin, eye
ACUTE TOXICITY LEVEL:
Moderately Toxic: ingestion
MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: eye disorders, immune system disorders or allergies, respiratory disorders, skin disorders and allergies

TRADE SECRET 00232322:
MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: high blood pressure, kidney disorders

Additional toxicological data is available on the component(s) of this product. Please call 650-638-5635 or contact MSDS_Inquiry_CCRM@appliedbiosystems.com for more information.

12. ECOLOGICAL INFORMATION

Not available

13. DISPOSAL CONSIDERATIONS

Dispose in accordance with all applicable regulations.

14. TRANSPORT INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION: No classification assigned.

CANADIAN TRANSPORTATION OF DANGEROUS GOODS: No classification assigned.

LAND TRANSPORT ADR: No classification assigned.

LAND TRANSPORT RID: No classification assigned.

AIR TRANSPORT IATA: No classification assigned.

AIR TRANSPORT ICAO: No classification assigned.

MARITIME TRANSPORT IMDG: No classification assigned.

15. REGULATORY INFORMATION

U.S. REGULATIONS:
SARA TITLE III SECTION 302 EXTREMELY HAZARDOUS SUBSTANCES (40 CFR 355.30):
Not regulated.

SARA TITLE III SECTION 304 EXTREMELY HAZARDOUS SUBSTANCES (40 CFR 355.40):
Not regulated.

SARA TITLE III SARA SECTIONS 311/312 HAZARDOUS CATEGORIES (40 CFR 370.21):
ACUTE: Yes
CHRONIC: No
FIRE: No
REACTIVE: No
SUDDEN RELEASE: No

SARA TITLE III SECTION 313 (40 CFR 372.65): Not regulated.

OSHA PROCESS SAFETY (29CFR1910.119): Not regulated.

STATE REGULATIONS:
California Proposition 65:
Known to the state of California to cause the following:
STRONG INORGANIC ACID MISTS CONTAINING SULFURIC ACID
Cancer (Mar 14, 2003)

CANADIAN REGULATIONS:

WHMIS CLASSIFICATION: This product has been classified in accordance with the hazard criteria of the CPR and the MSDS contains all of the information required by the CPR.

NATIONAL INVENTORY STATUS:

U.S. INVENTORY (TSCA): All the components of this substance are listed on or are exempt from the inventory. For purposes of 40 CFR 720.36, this product is for Research and Development (R&D) Use Only.

TSCA 12(b) EXPORT NOTIFICATION: Not listed.

16. OTHER INFORMATION

23.B. BIOPSY VISIT [V3] BLOOD PROCUREMENT AND PROCESSING PROCEDURES Pediatric and Adult Participants

Procedure Overview
This procedure describes the process for collecting and preparing blood samples obtained at the **[V3] Biopsy Visit** for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Requires Supplies:
Included in kit:

- 1 x 3.0 mL SST vacutainer[1] (Tube 19)
- 1 x 4.0 mL EDTA vacutainer[2] (Tube 14)
- 1 x RNA PAXgene vacutainer[3] (Tube 12)
- 3 pre-labeled cryovials[4]:
  - 2 red-capped cryovials to store serum from Tube 14
    Pre-labeled **B-E Blood EDTA (Red 1 and 2)**
  - 1 grey-capped cryovial to store serum from Tube 19
    Pre-labeled **B-S Blood SST (Gray**

Provided by site:

- Blood sample from study participant
- Aerosol spray covers for centrifuge buckets
- Pipettors and tips or disposable pipettes (1 ml or 200 µl sizes) or plastic transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:

- Centrifuge capable of achieving 2000 x g (NOTE: G is not the same as RPM, please consult your centrifuge conversion table if necessary)
- University of Michigan OSEH[5] guidelines designate all work done with biological specimens that could produce spray from pipetting is done in a hood.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated alternate would provide this service.

Procedure
When possible, blood should be drawn from the participant up to 7 days prior to the biopsy procedure. V3 Biopsy Visit blood may be obtained same day prior or same day post-procedure.

Note the date and start time of the blood draw on V3 Biopsy Specimens Worksheet.

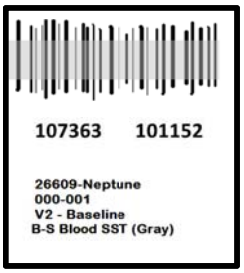
In accordance with the site's protocol for venipuncture, *draw blood tubes in order as follows*: 1 (one) 3.0 mL SST, 1 (one) 4.0 mL EDTA, and 1 (one) RNA PAXgene blood vacutainer from all participants, adult and pediatric.
Following the blood draw the Research Coordinator will return to the lab with the samples.

BLOOD PROCESSING FOR SST (RED/BLACK TIGER TOP) TUBE 19

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **[V3] Biopsy Visit** in SST blood tubes for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Required Supplies:
Included in kit:

- 1 x 3.0 mL SST blood vacutainer[1] (tube 19)
- 1 labeled cryovial[4] (**GRAY CAPS/GRAY LABELS**)
  (Pre-labeled **B-S Blood SST (Gray 3**)



Procedure
When possible, blood should be drawn from the participant up to 7 days prior to the biopsy procedure. V3 Biopsy Visit blood may be obtained same day prior or same day post-procedure.

Note the date and start time of the blood draw on V3 Biopsy Specimens Worksheet.

Sample processing:

1. Following the 30-minute incubation period, balance SST blood tubes per your site's centrifuge protocol and handling policy.
2. Note the time on the V3 Biospecimens worksheet (this should be the time the samples start to spin in the centrifuge).
3. Centrifuge SST tubes at 2000 x g for 12 minutes.

Tube 19

4. After spinning, remove tube from centrifuge keeping tubes upright so as not to disturb the serum*** component.
5. Pipette the serum layer from the SST tube (tube 19) into one approximate 1.6 mL aliquot. This amount can be determined by referencing Figure 1 from 26.A Appendix M Adult Blood Baseline V2. Use the cryovial labeled:

B-S Blood SST (Gray 3

6. Freeze aliquots at -80° C prior to shipping.
7. Discard remaining RBC's per site's OSEH guidelines. X

*** Serum is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance. Serum is not the same as plasma.

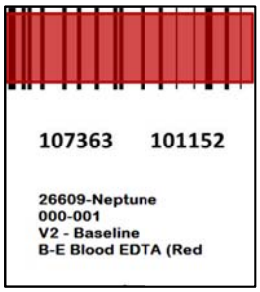
Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]**BIO-Blood

BLOOD PROCESSING FOR EDTA (PURPLE TOP) TUBE 14

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **[V3] Biopsy Visit** in EDTA blood tubes for NEPTUNE storage at -80° C. Shipping details are provided at the end of the blood processing MOP.

Required Supplies:
Included in kit:

- 1 x 4.0 mL EDTA blood vacutainer[2] tube (tubes 14)
- 2 labeled cryovials[4] (**RED CAPS/RED LABELS**)
  (Pre-labeled **B-E Blood EDTA (Red 1** and **B-E Blood EDTA (Red 2**)



Procedure
When possible, blood should be drawn from the participant up to 7 days prior to the biopsy procedure. V3 Biopsy Visit blood may be obtained same day prior or same day post-procedure.

Note the date and start time of the blood draw on V3 Biopsy Specimens Worksheet.

Sample processing:

1. Balance EDTA blood tube per site's centrifuge protocol and handling policy.
2. Note the time on the V3 Biospecimens worksheet (this should be the time the samples start to spin in the centrifuge).
3. Centrifuge EDTA tube at 2000 x g for 12 minutes.
4. Remove tubes from centrifuge keeping tubes upright so as not to disturb the plasma* component.
5. After spinning, pipette the plasma layer from the EDTA tube into two (2) approximate 1.6 mL aliquots. This amount can be determined by referencing Figure 1. Use the two cryovials labeled:

   B-E Blood EDTA (Red 1 and **B-E Blood EDTA (Red 2**
6. Freeze aliquots at -80° C prior to shipping.
7. Discard remaining RBC's per site's OSEH guidelines.

* Plasma is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance.

Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]**BIO-Blood

BLOOD PROCESSING FOR RNA PAXGENE (RED/CLEAR TOP) TUBE 12

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **[V3] Biopsy Visit** in RNA PAXgene blood tube for NEPTUNE storage at -80° C. Shipping details are provided at the end of the blood processing MOP.

Required Supplies:
Included in kit:

- 1 pre-labeled PAXgene RNA Blood Vacutainer^3 (**WHITE LABEL 'D RNA Paxgene (Whit'**) (Tube 12)

Required Equipment:

- No equipment is necessary for processing this specimen

Procedure
When possible, blood should be drawn from the participant up to 7 days prior to the biopsy procedure. V3 Biopsy Visit blood may be obtained same day prior or same day post-procedure.

Note the date and start time of the blood draw on V3 Biopsy Specimens Worksheet.

1. RNA blood vacutainer is marked with a **WHITE LABEL 'D RNA Paxgene (Whit'**

2. Blood draw:
   Summary:
   a. The PAXgene blood RNA vacutainer should be at room temperature prior to use.
   b. Fill the PAXgene RNA tube *after* all other tubes have been drawn.
   c. Collect blood into the PAXgene tube using your institution's recommended standard procedure for venipuncture.

   Blood Collection:
   a. Hold PAXgene tube vertically during blood draw, below point of venipuncture.
   b. Allow at least 10 seconds for complete blood draw; ensuring blood has stopped flowing into tube before removing from vacutainer holder.
   c. After blood collection gently invert tube 8-10 times.
   d. Store tube upright at room temperature for 2 hours.
   e. Following 2 hours room temperature incubation period, place in -80° C freezer upright.

Documentation
If PAXgene RNA tubes are left on shelf (room temp) for greater than 2 hour incubation period, please indicate additional elapsing time on the worksheet and case report forms. Additionally, if PAXgene RNA tubes stabilize at room temp for less than 2 hours, please indicate total time on worksheet and case report forms.

Complete the appropriate Biospecimen CRF corresponding to the study visit.

References

1. 3.5 mL SST Vacutainer: BD, Fisher Scientific ref No. 367981
2. 4.0 mL EDTA Vacutainer: BD, Fisher Scientific ref No. 367861
3. PreAnalytiX PAXgene Blood RNA Tube; 2.5 mL Vacutainer: ref. No. 762165 http://www.preanalytix.com/product-catalog/blood/rna/products/paxgene-blood-rna-tube/
4. Cryovials: DOT Scientific Inc. No. T334-6SPR
5. Follow local OSEH Guidelines
6. See attached MSDS for relevant safety precautions and hazards.

Centrifugation steps were performed in a SORVALL Legend T with radius 15.9 cm. If alternate centrifuges are used, the following equation may be used to calculate appropriate RPM necessary to generate the G-force indicated in above protocol:

$$RCF = 11.18 * \left(\frac{n}{1000}\right)^2 * r$$

RCF = Relative Centrifugal Force (G); a dimensionless number allowing comparison of separation efficiency

r = radius of centrifugation in cm

n = speed in rpm

Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]**BIO-Blood

Biopsy [V3] Blood Draw for Pediatric and Adult Participants

Tube #	Tube Type	Step 1	Step 2	Step 3	Step 4	Step 5
19	3.0 mL SST	Allow to clot for 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 1 cryovial.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
14	4 mL EDTA	Process within 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 2 cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
12	2.5 mL RNA	Must sit at room temp for 2 hours	Freeze at -80		Store pre-labeled vacutainer at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule

(Draw tubes in order as they appear in chart)

Procedure Class:	SPECIMENS
Procedure:	BIO-Spot Urine [V3: Biopsy] (SU, AS, AQ and AP)

Procedure Overview
This procedure describes the process for preparing one whole urine sample type (U), two urine supernatant sample types (S, Q) and 2 urine pellet sample types (AP-E and AP-Q) from a spot (random) urine sample for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Spot urine is collected in the same fashion for both pediatric and adult study participants. Spot urine samples are obtained at each study visit, including the baseline [V2] and the Biopsy [V3] visits, and all follow-up visits.

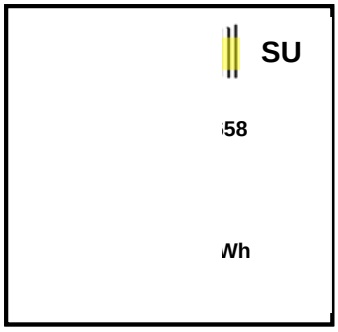
At [V3], the spot urine sample should be obtained PRIOR to the biopsy procedure. Please record this in the [V3] Biospecimen form.

Required Supplies:
Included in kit:

- 2 x 15.0 mL centrifuge tubes[1] empty (marked **"EMPTY"**)
- 2 x 15.0 mL centrifuge tubes containing 15 μL of Protease Inhibitor[2] (marked **"PI"**)
- 16 x 1.8 mL cryovials[3] with yellow caps
  (Pre-labeled as follows)

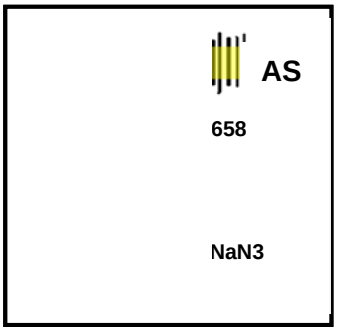
Sample 1:
SU = Whole, Unprocessed Urine

4 pre-labeled, empty cryovials
U-Spot Urine Spot Wh



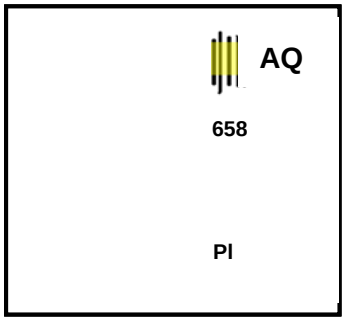
Sample 2:
AS = Processed & NaAzide

4 pre-labeled cryovials containing Sodium Azide[4]
AS Urine Spot SN NaN3



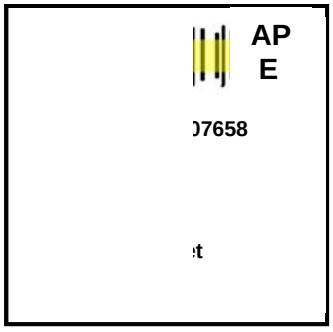
Sample 3:
AQ = Processed & Protease Inhibitor (PI)

4 pre-labeled cryovials for Protease Inhibitor
AQ Urine Spot SN PI



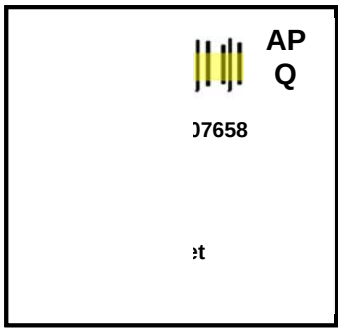
Sample 4:
AP-E = Urine Pellet from 'Empty' centrifuge tubes

2 pre-labeled, empty cryovials
AP-E Urine Pellet



Sample 5:
AP-Q = Urine Pellet from 'PI' containing centrifuge tubes

2 pre-labeled, empty cryovials
AP-Q Urine Pellet



- RNA-Later[5] (expected use per sample: 50-100 μL)

Provided by site:
- Spot Urine sample from study participant
- Pipettes and tips or disposable pipettes (10 ml, 5 ml, 1 ml sizes) or plastic Transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:
- Centrifuge capable of achieving 2000 x G
- University of Michigan OSEH guidelines designate all work done with biological specimens that could produce spray from pipetting be done in a hood. Please refer to your site specific OSEH policies.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving urine sample from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated, NEPTUNE trained alternate would provide this service.

Procedure:
1. Midstream urine is recovered in sterile specimen container and stored on ice. A minimum of 32 mL of urine is necessary.

2. Note time, fasting state and 1st, 2nd, 3rd, etc urine of the day on study visit worksheet (if patient is able to provide this detail, otherwise, indicate "No recall").

If processing is not able to be completed immediately, please store on ice or refrigerate for a maximum of 4 hours.

Sample processing:

Sample 1

*Requires total spot urine sample of 60 mL minimum; if sample is 50 mL or less please note in worksheet and CRF and do NOT store spot urine for the U-Spot Samples: * NO WHOLE URINE SAMPLE**

3. Using a pipettor, transfer ***whole***, unprocessed urine into the cryovials labeled:

'SU' to the right of the barcode

4. Replace the cap, firmly twisting in a clockwise direction.

Samples 2 & 3

5. Pour the remaining urine into the 4 x 15.0 mL centrifuge tubes in equal 12 milliliter portions (two tubes of each marked "EMPTY" and "Protease Inhibitor (PI)")

   E.g.:

   30 mL of spot urine → 2 – 12.0 mL centrifuge tubes for spinning (Use 1 'Empty' and 1 'PI' tube)

   50 mL of urine → 4 – 12.0 mL centrifuge tube; discard remaining urine (Use 2 of each, 'Empty' and 'PI')

NOTE: Use at least ONE EACH: "EMPTY" and "PI" centrifuge tubes

6. In the tubes labeled "PI", gently invert 8-10 times to dissolve the PI completely. Remove the cap to allow any air bubbles to escape, replace cap tightly.
7. Spin all 4 tubes at 1000 X G for 12 minutes in centrifuge

Sample 2 (AS Urine Spot): From the tubes labeled "EMPTY", transfer urine using a transfer pipettor into the 4 cryovials containing a pre-measured amount of 100 mM Sodium Azide (a biocide) labeled:

'AS' to the right of the barcode

8. When opening each cryovial, take care to place the cap directly in front of the respective tube to retain pre-measured volumes for consistent concentrations in each aliquot.
9. Pipette 1.6 mLs of urine or enough urine to fill the cryovial up to the first ridge on the cryovial (see Figure 1).
10. Replace the cap, firmly twisting in a clockwise direction. After all caps are replaced, invert tubes *at least 2 times* to distribute the sodium azide prior to freezing.

Sample 3 (AQ Urine Spot): From the tubes labeled "PI", transfer urine using a transfer pipettor into the cryovials labeled:

'AQ' to the right of the barcode

11. Pipette 1.6 mLs of urine or enough urine to fill the cryovial up to the first ridge on the cryovial (see Figure 1).

Samples 4 and 5

12. Pour off remaining supernatant from all of the 15.0 mL centrifuge tubes
13. For maximal drainage, gently invert centrifuge tubes on clean paper towels for 10 seconds, take care to not disturb pellet in the centrifuge tube tip.
14. With a clean pipette tip, transfer 25.0-50.0* μL RNA-Later into each centrifuge tube, take care to not touch the inside walls of the centrifuge tube.
15. Gently stir the mixture with the pipette tip, changing tips when moving between the 'Empty' tubes and the 'PI' tubes. **Do not pipette up and down to mix as this could break any cells present in the pellet.**

    Sample 4 (AP-E Urine Pellet): From the centrifuge tubes labeled "EMPTY", pipette one urine pellet from each centrifuge tube into the two cryovials labeled:

    'AP-E' to the right of the barcode

    Sample 5 (AP-Q Urine Pellet): From the centrifuge tubes labeled "PI", pipette one urine pellet from each centrifuge tube into the two cryovials labeled:

    'AP-Q' to the right of the barcode

16. Freeze all samples at -80 C.
17. Residual urine may be disposed per OSEH guidelines enforced at participating institution.

* Amount of RNA-Later will vary depending on size of pellet. RNA-Later should be added to completely submerse the pellet.

Shipping
Samples should be shipped according to the site-specific scheduled interval for shipments.

All specimens should be shipped together **on dry ice** using the shipping instructions found in Appendix N and in the study specific container provided by NEPTUNE.

Documentation
All corresponding samples for each participant ID should be stored together. If specimen does not adequately fill pre-determined number of aliquots, please document to minimize concerns regarding lost aliquots.

Complete the appropriate Biospecimen CRF corresponding to the study visit.

Procedure Class:	SPECIMENS
Procedure:	BIO-Spot Urine [V3: Biopsy] (SU, AS, AQ and AP)

References

1. 15.0 mL orange-capped Corning centrifuge tubes: Fisher Scientific No. 05-538-53D, Corning No. 430052
2. Protease Inhibitor Cocktail: Sigma-Aldrich Catalog: P1860 – 1 mL
3. Cryovials: DOT Scientific Inc. No.: T334-6SPR
4. Sodium Azide (see attached MSDS)
5. Ambion RNA-Later Solution; P/N: Am7021
6. University of Michigan Occupations Safety and Environmental Health (OSEH) guidelines indicate washing urine and its debris down laboratory sink with adequate water.

Relevant Definitions: NaN_3: Sodium Azide

27. Appendix N. Shipping

27.A. Shipments with Biological Substances Category B ("Full" specimen kits)

For the purposes of NEPTUNE, shipments with "Biological Substances, Category B" will be sent from participating NEPTUNE sites to the University of Michigan.

These shipments contain processed blood, urine and kidney tissue specimens for use by the NEPTUNE study.

27.B. Maximum Kits Per Shipment

Shipments may contain up to 4 baseline kits and/or 6 return visits for a **maximum combined total of up to 6 kits per shipment**. More than one visit from the same participant should not be combined in a single shipment. Shipments containing "full" specimen kits will be packaged in the following manner.

27.C. Items Required for Proper Shipment

27.C.1. Study Provided

- NEPTUNE styrofoam box
- NEPTUNE cardboard box
- 95 kPa pressure tested bags
- Specimen kits sealed in provided biohazard specimen bags with orange study ID inserts
- NEPTUNE Shipping Manifest
- Dry Ice and Biological Substances, Class B Labels

27.C.2. Site Provided

- 4.5 kg of dry ice (about the weight of a gallon of milk)
- Packing tape
- Absorbent material (e.g. paper towel)

27.D. Shipment Preparation Instructions

1. Wrap PAXgene tubes individually in absorbent material (paper towel or absorbent sleeves sent with the NEPTUNE kits).
2. Place wrapped PAXgene tubes and blood cryovials in the **"Blood"** (red barcoded) biohazard specimen bag and all urine cryovials and tubes in the **"Urine"** (yellow barcoded) biohazard specimen bag
3. Place absorbent material (paper towel) in the specimen bags and close by pressing the zipper seal.
4. Place the pre-labeled specimen bags into a 95 kPa pressure tested bag and seal per the manufacturer's instructions on page 4).
5. Place ½ of the total dry ice at the bottom of the Styrofoam box.
6. Place the specimen-filled 95 kPa pressure tested bags on top of the dry ice.
7. Place the remaining ½ of dry ice on top of the 95 kPa pressure tested bags.
8. Place the lid on the Styrofoam box.

Do not tape the Styrofoam box shut!

9. Place the Styrofoam box into the cardboard box.
10. If nail specimens need to be shipped, they are to be placed **outside and on top of the Styrofoam box**, prior to taping the cardboard box closed.
11. Close and tape the cardboard box for shipping while making sure **not** to seal all box edges. This will allow CO2 released from the dry ice to escape the package.
12. Weigh the cardboard box and note the weight.
13. Attach the Biological Specimens Category B and Dry Ice labels to the cardboard box.
14. Record the weight of the dry ice on the Dry Ice label.

27.E. UPS Shipment Instructions – Biological Specimens

The NEPTUNE Data Analysis and Coordinating Center has created an account for shipping NEPTUNE materials via UPS, with access for creating and billing shipments through the internet. If your site is not scheduled for regular UPS pick-ups, please schedule a pick-up as indicated in the on-line shipment guide below.

27.E.1. Creating a UPS Shipment for pick-up and invoice

1. Go to UPS link:
   https://www.campusship.ups.com/login/umstrategiccon
2. Sign in using the following information:
   Username: boridley
   Password: NEPTUNE

   You will be prompted by the "Begin Your Shipment" box.
3. Box #1
   a) "Where is the shipment going?"
   b) Select the shipment's destination "NEPTUNE Biorepository" by using the drop down box located under "Address Book."
4. Box #2
   c) "Where is the shipment coming from?"
   d) Click on the "Edit" link:
   Using the drop down box located under "Address Book", select your location and name. Make sure the address is correct. If not correct, please contact Kyle at spottsk@umich.edu
   e) Scroll down and click on the "Update" button at the bottom right-hand side of the "Address Information" box.

   You should now see the "Begin Your Shipment" box.
5. Box #3
   f) "What are you shipping?"
   g) Select the number of packages from the drop down box.
   h) Under "Packaging Type", select "Other Packaging".
   i) Under "Weight" Enter the weight of your package in pounds (lbs.)
6. Box #4
   j) "How would you like to ship?"
   k) Using the drop down box that says "Select Service," choose Next Day Air. All Category B Biological Substances must be sent via Next Day Air.
   l) Make sure the "Send E-mail Notifications" and "Dry Ice" boxes have check marks.

7. Box #5 “Would you like to add reference numbers to this shipment?”
   Enter 062136 under “Short code Required” if it didn’t automatically populate.
8. Box #6 “How would you like to pay?”
   Select “A07R07 – Internal Medicine/Nephrology” if it didn’t automatically populate
9. Box #7 “Would you like to schedule a pick-up?”
   If your site has a daily UPS shipment pick-up, please use it. Otherwise, you will need to check the “Schedule a Pickup” box or drop off the package at a UPS store.

   Click “Next”
10. A new #1 box “Send E-mail Notifications Using Quantum View Notify” should appear
    Enter your email address, the person you are shipping to, and spottks@umich.edu into the fields if not automatically populated.
    Check the “Ship”, “Exception” and “Delivery” column boxes for all the email addresses.
11. Under “Personal E-mail Message:” enter a list of all kits contained within the shipment.
    For Example: BL: 000-007, 001-008 RV5: 000-003 RV6: 000-001
12. Box #2 Dry Ice
    Enter the amount of dry ice added to the shipping box in lbs or kg. The amount of dry ice required is 4.5kg or 9.9lbs (about the weight of a gallon of milk).

    Click “Next”
13. A screen will prompt you to “Review your shipment details.” Please make sure all of the information on this page is correct then click “Ship Now” at the bottom right corner of the box.
14. Your printer dialogue box should appear (pop-ups must be enabled).
15. Please print the shipping label and the receipt.
16. Cut or fold the shipping label to fit the NEPTUNE box.
17. Tape the shipping label to the top of the NEPTUNE box.
18. Keep the receipt for your records.
19. Your package is ready to ship!

CLOSING INSTRUCTIONS
FOR THESE VONSEAL® SPECIMEN SHIPPING BAGS

The specimen shipping bags in this carton are designed to perform at high internal pressure should an airliner lose it's cabin pressure.

In order for the bag to perform to it's design capabilities, it is imperative that the bag be closed properly after insertion of the specimen.

PLEASE FOLLOW THE PROCEDURES ILLUSTRATED BELOW

FIG. #1

Figure 1: shows the bag laying flat on a counter with the tape side up and the tape end towards the person closing the bag.

FIG. #2

Figure 2: shows the specimen at the bottom of the bag and the area above the specimen being flattened in preparation for the adhesive tape to fold over.

FIG. #3

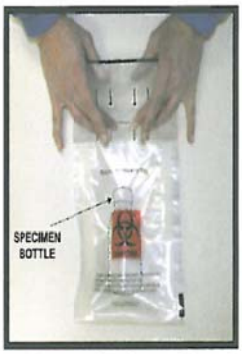


Figure 3: shows the bag after the paper adhesive cover has been removed and with the middle fingers touching the adhesive at the middle of the bag below the slit opening. It also shows the thumbs under the end of the bag ready to fold the top of the bag over.

FIG. #4

Figure 4: shows the bag after the top is folded at the slit opening and the thumbs pressing the folded end of the bag.

FIG #5

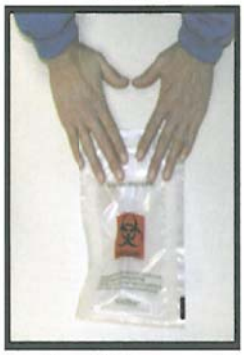


Figure 5: shows the middle finger of both hands being used to press the adhesive together. Start at the center of the fold and work outward. Please be sure to firmly press the entire adhesive area, especially the folded edge and corners.

This is a high performance bag. Thank you for making the effort to close it properly.

27.F. Pathology Slide/Materials Shipping

For the purposes of NEPTUNE, biopsy slide shipments will be sent from participating NEPTUNE sites to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

These shipments are considered non-biological specimens. Dry ice and special shipping precautions are not necessary.

Please be sure pathology materials are properly de-identified, including any letterhead information, physician names, etc. as specified in 15. Appendix B Pathology Manual of Procedures.

27.G. Items Required for Proper Shipment

27.G.1. Study Provided

- Padded, bubble mailer
- Slide holders
- Blank CD

27.G.2. Site Provided

- Study labeled and de-identified NEPTUNE participant slides
- Study labeled CD with de-identified EM and path report data
- Hardcopy de-identified pathology report with Participant Study ID

27.H. Shipment Preparation Instructions

1. Place labeled and de-identified slides in provided slide holders
2. Label each slide holder with the correct participant ID
3. Place all slide holders that will comfortably fit in the provided bubble mailing envelope and seal.

27.I. UPS Shipment Instructions – Non-Biological Specimens

The NEPTUNE Data Analysis and Coordinating Center has created an account for shipping NEPTUNE materials via UPS, with access for creating and billing shipments through the internet. If your site is not scheduled for regular UPS pick-ups, please schedule a pick-up as indicated in the shipment guide below.

27.I.1. Creating a UPS Shipment for pick-up and invoice

1. Go to UPS link:
   https://www.campusship.ups.com/login/umstrategiccon

2. Sign in using the following information:
   Username: boridley
   Password: NEPTUNE

   You will be prompted by the “Begin Your Shipment” box.

3. Box #1
   “Where is the shipment going?”
   m) Select the shipment’s destination “**Lisa Swearinger - NIH”** by using the drop down box located under “**Address Book**.”

4. Box #2
   "Where is the shipment coming from?"
   n) Click on the "Edit" link:

      Using the drop down box located under "Address Book", select your location and name. Make sure the address is correct. If not correct, please contact Kyle at spottsk@umich.edu
   o) Scroll down and click on the "Update" button at the bottom right-hand side of the "Address Information" box.

   You should now see the "Begin Your Shipment" box.

5. Box #3
   "What are you shipping?"
   p) Select the number of packages from the drop down box.
   q) Under "Packaging Type", select "Other Packaging".
   r) Under "Weight" Enter the weight of your package in pounds (lbs.)

6. Box #4
   "How would you like to ship?"
   s) Using the drop down box that says "Select Service," please select "ground".
   t) Make sure the "Send E-mail Notifications" box has a check mark.

7. Box #5
   "Would you like to add reference numbers to this shipment?"
   u) Enter 062136 under "Short code Required" if this information did not auto-populate.

8. Box #6
   "How would you like to pay?"
   v) Select "A07R07 – Internal Medicine/Nephrology" if this information did not auto-populate.

9. Box #7
   "Would you like to schedule a pick-up?"
   w) If your site has a daily UPS shipment pick-up, please use it. Otherwise, you will need to check the "Schedule a Pickup" box or drop off the package at a UPS store.

   Click "Next"

10. A new #1 box "Send E-mail Notifications Using Quantum View Notify" should appear
    If not automatically populated, enter:
    x) Your email address
    y) The person you are shipping to (Lisa Swearinger - NIH), and spottsk@umich.edu into the fields if not automatically populated.
    z) Check the "Ship", "Exception" and "Delivery" column boxes for all the email addresses.

11. Under "Personal E-mail Message:" enter a list of all participant ID slides contained within the shipment.
    For Example: 000-001 through 000-004

Click “Next”

12. A screen will prompt you to “Review your shipment details.” Please make sure all of the information on this page is correct then click “Ship Now” at the bottom right corner of the box.

13. Your printer dialogue box should appear (you may need to enable pop-ups if previously disabled).

14. Please print the shipping label and the receipt.

15. Cut or fold the shipping label to fit the bubble mailer.

16. Tape the shipping label to the top of the bubble mailer.

17. Keep the receipt for your records.

18. Your package is ready to ship!

27.J. International Shipping

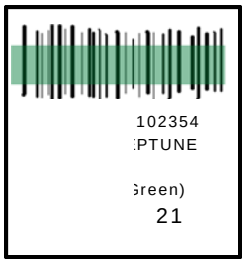
Please discuss with the NEPTUNE DACC for international shipping considerations.

Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]** BIOPSY TISSUE

Procedure Overview
This procedure describes the process for storing renal biopsy tissue for the NEPTUNE Biobank at -80° C. Shipping details are provided in 27. Appendix N Shipping.

Required Supplies:
Included in kit:

- 1 pre-labeled cryovial[1] containing 1.6 mL RNA-Later[2]



Provided by site:

- Renal tissue sample from study participant
- Gloves, goggles, and lab coat

Required Equipment:

- No equipment is necessary for this specimen

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, Site PI or designated individual would serve as alternates.

Only a nephrologist or other trained healthcare professional is able to do the renal biopsy.

Procedure
The green-labeled, green-capped cryovial containing RNA-Later MUST be present during the biopsy procedure. Specimen must be placed directly into RNA-later and not be immersed in other fixative solutions prior to storage.

1. Attending physician will procure the renal tissue core during procedure
2. In sterile fashion, the attending physician will procure one full core from specimens obtained
3. In sterile fashion, place the specimen in the green-labeled, green capped cryovial and place lid on, rotating cap to the right to close completely.
4. The specimen in RNA-Later solution is stable at room temperature until return to lab.

Shipping:
Biopsy specimens should be stored with the respective NEPTUNE Participant samples. If Baseline [V2] has not yet occurred, please take care in storing the single cryovial in a -80 freezer. Samples should be shipped with the respective kit.

All specimens should be shipped together **on dry ice** using the NEPTUNE shipping vendor and container provided by the NEPTUNE DACC/Biobank.

Documentation
All corresponding samples for each participant number should be stored together. Please note, effective 6/2012 the number of passes to obtain the research core must be documented in Kidney Specimens Worksheet 11A and documented in the corresponding CRF.

References
1. Cryovials: DOT Scientific Inc. No. T334-6SPR
2. See attached MSDS

Relevant Definitions
None

BIOPSY VISIT [V3] BLOOD PROCUREMENT AND PROCESSING PROCEDURES
Pediatric and Adult Participants

Procedure Overview
This procedure describes the process for collecting and preparing blood samples obtained at the **[V3] Biopsy Visit** for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Requires Supplies:
Included in kit:

- 1 x 3.0 mL SST vacutainer[1] (Tube 19)
- 1 x 4.0 mL EDTA vacutainer[2] (Tube 14)
- 1 x RNA PAXgene vacutainer[3] (Tube 12)
- 3 pre-labeled cryovials[4]:
  - 2 red-capped cryovials to store serum from Tube 14
    Pre-labeled **B-E Blood EDTA (Red 1 and 2)**
  - 1 grey-capped cryovial to store serum from Tube 19
    Pre-labeled **B-S Blood SST (Gray**

Provided by site:

- Blood sample from study participant
- Aerosol spray covers for centrifuge buckets
- Pipettors and tips or disposable pipettes (1 ml or 200 µl sizes) or plastic transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:

- Centrifuge capable of achieving 2000 x g (NOTE: G is not the same as RPM, please consult your centrifuge conversion table if necessary)
- University of Michigan OSEH[5] guidelines designate all work done with biological specimens that could produce spray from pipetting is done in a hood.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated alternate would provide this service.

Procedure
When possible, blood should be drawn from the participant up to 7 days prior to the biopsy procedure. V3 Biopsy Visit blood may be obtained same day prior or same day post-procedure.

Note the date and start time of the blood draw on V3 Biopsy Specimens Worksheet.

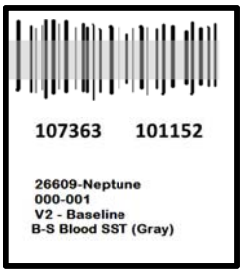
In accordance with the site's protocol for venipuncture, *draw blood tubes in order as follows*: 1 (one) 3.0 mL SST, 1 (one) 4.0 mL EDTA, and 1 (one) RNA PAXgene blood vacutainer from all participants, adult and pediatric.
Following the blood draw the Research Coordinator will return to the lab with the samples.

BLOOD PROCESSING FOR SST (RED/BLACK TIGER TOP) TUBE 19

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **[V3] Biopsy Visit** in SST blood tubes for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Required Supplies:
Included in kit:

- 1 x 3.0 mL SST blood vacutainer[1] (tube 19)
- 1 labeled cryovial[4] (**GRAY CAPS/GRAY LABELS**)
  (Pre-labeled **B-S Blood SST (Gray 3**)



Procedure
When possible, blood should be drawn from the participant up to 7 days prior to the biopsy procedure. V3 Biopsy Visit blood may be obtained same day prior or same day post-procedure.

Note the date and start time of the blood draw on V3 Biopsy Specimens Worksheet.

Sample processing:

1. Following the 30-minute incubation period, balance SST blood tubes per your site's centrifuge protocol and handling policy.
2. Note the time on the V3 Biospecimens worksheet (this should be the time the samples start to spin in the centrifuge).
3. Centrifuge SST tubes at 2000 x g for 12 minutes.

Tube 19

4. After spinning, remove tube from centrifuge keeping tubes upright so as not to disturb the serum*** component.
5. Pipette the serum layer from the SST tube (tube 19) into one approximate 1.6 mL aliquot. This amount can be determined by referencing Figure 1 from 26.A Appendix M Adult Blood Baseline V2. Use the cryovial labeled:

B-S Blood SST (Gray 3

6. Freeze aliquots at -80° C prior to shipping.
7. Discard remaining RBC's per site's OSEH guidelines. X

*** Serum is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance. Serum is not the same as plasma.

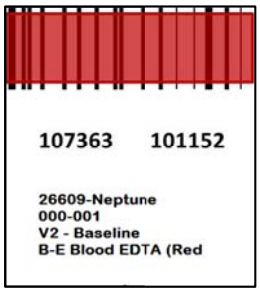
Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]**BIO-Blood

BLOOD PROCESSING FOR EDTA (PURPLE TOP) TUBE 14

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **[V3] Biopsy Visit** in EDTA blood tubes for NEPTUNE storage at -80° C. Shipping details are provided at the end of the blood processing MOP.

Required Supplies:
Included in kit:

- 1 x 4.0 mL EDTA blood vacutainer[2] tube (tubes 14)
- 2 labeled cryovials[4] (**RED CAPS/RED LABELS**)
  (Pre-labeled **B-E Blood EDTA (Red 1** and **B-E Blood EDTA (Red 2**)



Procedure
When possible, blood should be drawn from the participant up to 7 days prior to the biopsy procedure. V3 Biopsy Visit blood may be obtained same day prior or same day post-procedure.

Note the date and start time of the blood draw on V3 Biopsy Specimens Worksheet.

Sample processing:

1. Balance EDTA blood tube per site's centrifuge protocol and handling policy.
2. Note the time on the V3 Biospecimens worksheet (this should be the time the samples start to spin in the centrifuge).
3. Centrifuge EDTA tube at 2000 x g for 12 minutes.
4. Remove tubes from centrifuge keeping tubes upright so as not to disturb the plasma* component.
5. After spinning, pipette the plasma layer from the EDTA tube into two (2) approximate 1.6 mL aliquots. This amount can be determined by referencing Figure 1. Use the two cryovials labeled:

   B-E Blood EDTA (Red 1 and **B-E Blood EDTA (Red 2**
6. Freeze aliquots at -80° C prior to shipping.
7. Discard remaining RBC's per site's OSEH guidelines.

* Plasma is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance.

Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]**BIO-Blood

BLOOD PROCESSING FOR RNA PAXGENE (RED/CLEAR TOP) TUBE 12

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **[V3] Biopsy Visit** in RNA PAXgene blood tube for NEPTUNE storage at -80° C. Shipping details are provided at the end of the blood processing MOP.

Required Supplies:
Included in kit:

- 1 pre-labeled PAXgene RNA Blood Vacutainer[3] (**WHITE LABEL 'D RNA Paxgene (Whit'**) (Tube 12)

Required Equipment:

- No equipment is necessary for processing this specimen

Procedure
When possible, blood should be drawn from the participant up to 7 days prior to the biopsy procedure. V3 Biopsy Visit blood may be obtained same day prior or same day post-procedure.

Note the date and start time of the blood draw on V3 Biopsy Specimens Worksheet.

1. RNA blood vacutainer is marked with a **WHITE LABEL 'D RNA Paxgene (Whit'**

2. Blood draw:
   Summary:
   a. The PAXgene blood RNA vacutainer should be at room temperature prior to use.
   b. Fill the PAXgene RNA tube *after* all other tubes have been drawn.
   c. Collect blood into the PAXgene tube using your institution's recommended standard procedure for venipuncture.

   Blood Collection:
   a. Hold PAXgene tube vertically during blood draw, below point of venipuncture.
   b. Allow at least 10 seconds for complete blood draw; ensuring blood has stopped flowing into tube before removing from vacutainer holder.
   c. After blood collection gently invert tube 8-10 times.
   d. Store tube upright at room temperature for 2 hours.
   e. Following 2 hours room temperature incubation period, place in -80° C freezer upright.

Documentation
If PAXgene RNA tubes are left on shelf (room temp) for greater than 2 hour incubation period, please indicate additional elapsing time on the worksheet and case report forms. Additionally, if PAXgene RNA tubes stabilize at room temp for less than 2 hours, please indicate total time on worksheet and case report forms.

Complete the appropriate Biospecimen CRF corresponding to the study visit.

Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]**BIO-Blood

References

1. 3.5 mL SST Vacutainer: BD, Fisher Scientific ref No. 367981
2. 4.0 mL EDTA Vacutainer: BD, Fisher Scientific ref No. 367861
3. PreAnalytiX PAXgene Blood RNA Tube; 2.5 mL Vacutainer: ref. No. 762165 http://www.preanalytix.com/product-catalog/blood/rna/products/paxgene-blood-rna-tube/
4. Cryovials: DOT Scientific Inc. No. T334-6SPR
5. Follow local OSEH Guidelines
6. See attached MSDS for relevant safety precautions and hazards.

Centrifugation steps were performed in a SORVALL Legend T with radius 15.9 cm. If alternate centrifuges are used, the following equation may be used to calculate appropriate RPM necessary to generate the G-force indicated in above protocol:

$$RCF = 11.18 * \left(\frac{n}{1000}\right)^2 * r$$

RCF = Relative Centrifugal Force (G); a dimensionless number allowing comparison of separation efficiency

r = radius of centrifugation in cm

n = speed in rpm

Procedure Class:	SPECIMENS
Procedure:	**BIOPSY VISIT [V3]**BIO-Blood

Biopsy [V3] Blood Draw for Pediatric and Adult Participants

Tube #	Tube Type	Step 1	Step 2	Step 3	Step 4	Step 5
19	3.0 mL SST	Allow to clot for 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 1 cryovial.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
14	4 mL EDTA	Process within 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 2 cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
12	2.5 mL RNA	Must sit at room temp for 2 hours	Freeze at -80		Store pre-labeled vacutainer at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule

(Draw tubes in order as they appear in chart)

Procedure Class:	SPECIMENS
Procedure:	BIO-Spot Urine [V3: Biopsy] (SU, AS, AQ and AP)

Procedure Overview
This procedure describes the process for preparing one whole urine sample type (U), two urine supernatant sample types (S, Q) and 2 urine pellet sample types (AP-E and AP-Q) from a spot (random) urine sample for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Spot urine is collected in the same fashion for both pediatric and adult study participants. Spot urine samples are obtained at each study visit, including the baseline [V2] and the Biopsy [V3] visits, and all follow-up visits.

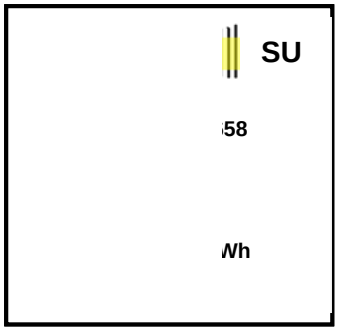
At [V3], the spot urine sample should be obtained PRIOR to the biopsy procedure. Please record this in the [V3] Biospecimen form.

Required Supplies:
Included in kit:

- 2 x 15.0 mL centrifuge tubes[1] empty (marked **"EMPTY"**)
- 2 x 15.0 mL centrifuge tubes containing 15 μL of Protease Inhibitor[2] (marked **"PI"**)
- 16 x 1.8 mL cryovials[3] with yellow caps
  (Pre-labeled as follows)

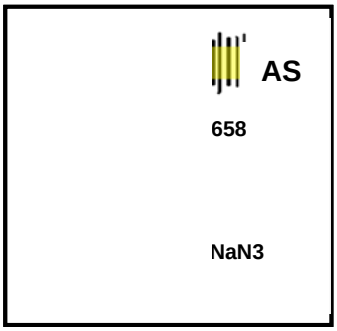
Sample 1:
SU = Whole, Unprocessed Urine

4 pre-labeled, empty cryovials
U-Spot Urine Spot Wh



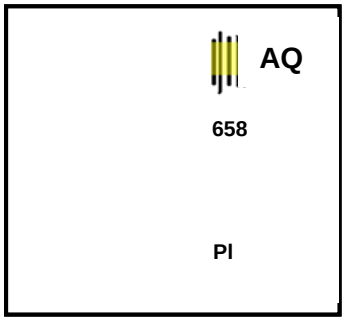
Sample 2:
AS = Processed & NaAzide

4 pre-labeled cryovials containing Sodium Azide[4]
AS Urine Spot SN NaN3



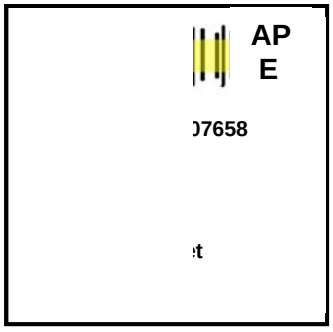
Sample 3:
AQ = Processed & Protease Inhibitor (PI)

4 pre-labeled cryovials for Protease Inhibitor
AQ Urine Spot SN PI



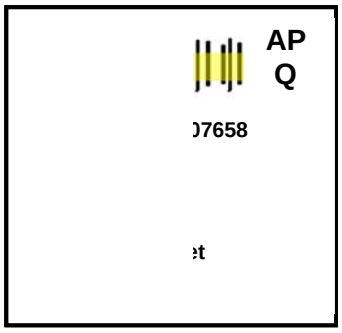
Sample 4:
AP-E = Urine Pellet from 'Empty' centrifuge tubes

2 pre-labeled, empty cryovials
AP-E Urine Pellet



Sample 5:
AP-Q = Urine Pellet from 'PI' containing centrifuge tubes

2 pre-labeled, empty cryovials
AP-Q Urine Pellet



- RNA-Later[5] (expected use per sample: 50-100 μL)

Provided by site:
- Spot Urine sample from study participant
- Pipettes and tips or disposable pipettes (10 ml, 5 ml, 1 ml sizes) or plastic Transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:
- Centrifuge capable of achieving 2000 x G
- University of Michigan OSEH guidelines designate all work done with biological specimens that could produce spray from pipetting be done in a hood. Please refer to your site specific OSEH policies.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving urine sample from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated, NEPTUNE trained alternate would provide this service.

Procedure:
1. Midstream urine is recovered in sterile specimen container and stored on ice. A minimum of 32 mL of urine is necessary.

2. Note time, fasting state and 1st, 2nd, 3rd, etc urine of the day on study visit worksheet (if patient is able to provide this detail, otherwise, indicate "No recall").

If processing is not able to be completed immediately, please store on ice or refrigerate for a maximum of 4 hours.

Sample processing:

Sample 1

*Requires total spot urine sample of 60 mL minimum; if sample is 50 mL or less please note in worksheet and CRF and do NOT store spot urine for the U-Spot Samples: * NO WHOLE URINE SAMPLE**

3. Using a pipettor, transfer ***whole***, unprocessed urine into the cryovials labeled:

'SU' to the right of the barcode

4. Replace the cap, firmly twisting in a clockwise direction.

Samples 2 & 3

5. Pour the remaining urine into the 4 x 15.0 mL centrifuge tubes in equal 12 milliliter portions (two tubes of each marked "EMPTY" and "Protease Inhibitor (PI)")

   E.g.:

   30 mL of spot urine → 2 – 12.0 mL centrifuge tubes for spinning (Use 1 'Empty' and 1 'PI' tube)

   50 mL of urine → 4 – 12.0 mL centrifuge tube; discard remaining urine (Use 2 of each, 'Empty' and 'PI')

NOTE: Use at least ONE EACH: "EMPTY" and "PI" centrifuge tubes

6. In the tubes labeled "PI", gently invert 8-10 times to dissolve the PI completely. Remove the cap to allow any air bubbles to escape, replace cap tightly.
7. Spin all 4 tubes at 1000 X G for 12 minutes in centrifuge

Sample 2 (AS Urine Spot): From the tubes labeled "EMPTY", transfer urine using a transfer pipettor into the 4 cryovials containing a pre-measured amount of 100 mM Sodium Azide (a biocide) labeled:

'AS' to the right of the barcode

8. When opening each cryovial, take care to place the cap directly in front of the respective tube to retain pre-measured volumes for consistent concentrations in each aliquot.
9. Pipette 1.6 mLs of urine or enough urine to fill the cryovial up to the first ridge on the cryovial (see Figure 1).
10. Replace the cap, firmly twisting in a clockwise direction. After all caps are replaced, invert tubes *at least 2 times* to distribute the sodium azide prior to freezing.

Sample 3 (AQ Urine Spot): From the tubes labeled "PI", transfer urine using a transfer pipettor into the cryovials labeled:

'AQ' to the right of the barcode

11. Pipette 1.6 mLs of urine or enough urine to fill the cryovial up to the first ridge on the cryovial (see Figure 1).

Samples 4 and 5

12. Pour off remaining supernatant from all of the 15.0 mL centrifuge tubes
13. For maximal drainage, gently invert centrifuge tubes on clean paper towels for 10 seconds, take care to not disturb pellet in the centrifuge tube tip.
14. With a clean pipette tip, transfer 25.0-50.0* μL RNA-Later into each centrifuge tube, take care to not touch the inside walls of the centrifuge tube.
15. Gently stir the mixture with the pipette tip, changing tips when moving between the 'Empty' tubes and the 'PI' tubes. **Do not pipette up and down to mix as this could break any cells present in the pellet.**

    Sample 4 (AP-E Urine Pellet): From the centrifuge tubes labeled "EMPTY", pipette one urine pellet from each centrifuge tube into the two cryovials labeled:

    'AP-E' to the right of the barcode

    Sample 5 (AP-Q Urine Pellet): From the centrifuge tubes labeled "PI", pipette one urine pellet from each centrifuge tube into the two cryovials labeled:

    'AP-Q' to the right of the barcode

16. Freeze all samples at -80 C.
17. Residual urine may be disposed per OSEH guidelines enforced at participating institution.

* Amount of RNA-Later will vary depending on size of pellet. RNA-Later should be added to completely submerse the pellet.

Shipping
Samples should be shipped according to the site-specific scheduled interval for shipments.

All specimens should be shipped together **on dry ice** using the shipping instructions found in Appendix N and in the study specific container provided by NEPTUNE.

Documentation
All corresponding samples for each participant ID should be stored together. If specimen does not adequately fill pre-determined number of aliquots, please document to minimize concerns regarding lost aliquots.

Complete the appropriate Biospecimen CRF corresponding to the study visit.

Procedure Class:	SPECIMENS
Procedure:	BIO-Spot Urine [V3: Biopsy] (SU, AS, AQ and AP)

References

1. 15.0 mL orange-capped Corning centrifuge tubes: Fisher Scientific No. 05-538-53D, Corning No. 430052
2. Protease Inhibitor Cocktail: Sigma-Aldrich Catalog: P1860 – 1 mL
3. Cryovials: DOT Scientific Inc. No.: T334-6SPR
4. Sodium Azide (see attached MSDS)
5. Ambion RNA-Later Solution; P/N: Am7021
6. University of Michigan Occupations Safety and Environmental Health (OSEH) guidelines indicate washing urine and its debris down laboratory sink with adequate water.

Relevant Definitions: NaN_3: Sodium Azide

Procedure Class:	SPECIMENS
Procedure:	**BASELINE [V2] ADULT** BIO-Blood (BB, BRF, BS, BSF, BG, BE)

26.A.1. UPDATES TO BLOOD BIOSPECIMEN PROCESSING PROCEDURES:

1. Effective 11/2012 NEPTUNE will use light sensitive dark cryovials in place of the previously used light sensitive eppendorf tubes (conical bottom). Throughout the MOP, these new cryovials will be referred to as the 'dark cryovials'.

   The volume requested for filling dark cryovials is the same as the clear cryovials: 1.6 mLs.

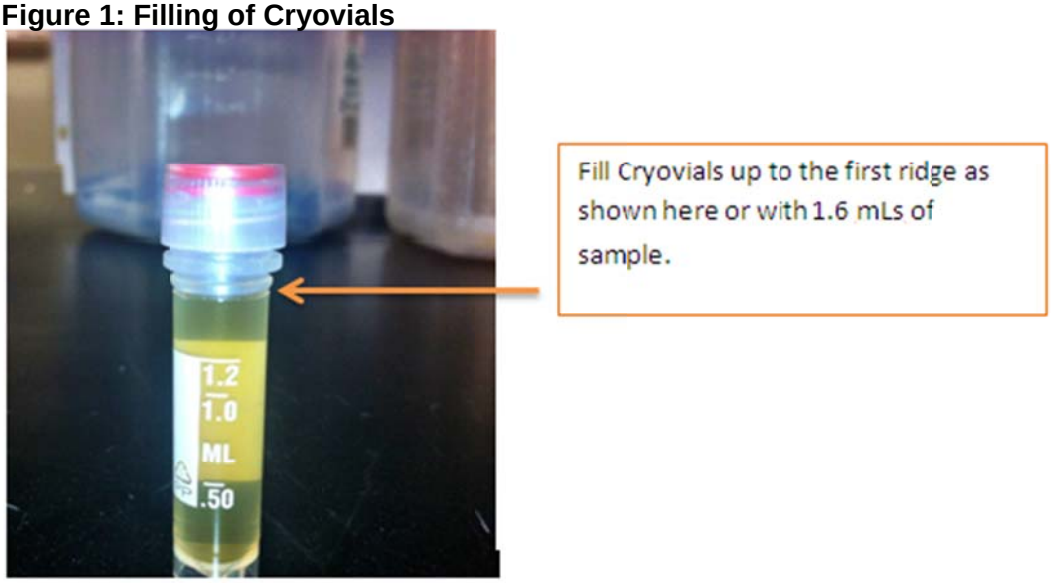
2. Research Coordinators (RCs) will no longer fill sets of cryovials with equal volumes of sample. Effective 11/2012 please fill each cryovial with the maximum volume (1.6 mL) in sequential order (based on the aliquot number indicated on barcoded label) until all corresponding sample in the blood draw tube(s) has been aliquotted. Discard remaining empty cryovials on-site.

3. When transferring blood plasma/serum samples from the blood draw tubes into cryovials for freezer storage, it is imperative that these containers are not overfilled. The following procedures take into account liquid expansion when samples freeze.

   a) <u>Filling cryovials with biospecimens:</u>

   - Digital pipettors: Transfer a total of 1.6 mls of sample into the cryovials.
   - Transfer pipettes (disposable, plastic): Note the two ridges below the cap of the cryovial. Use the lower ridge as a reference point for filling cryovials. Please see Figure 1 below.

Figure 1: Filling of Cryovials



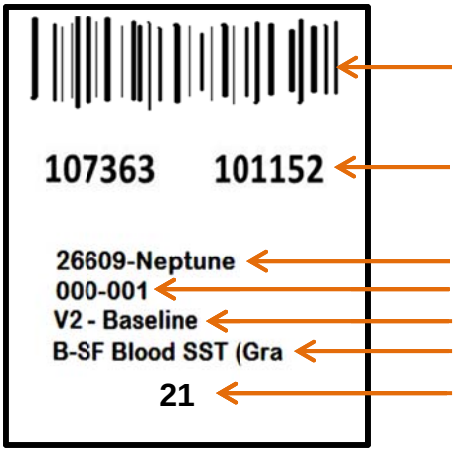
   b) <u>Filling the dark cryovials:</u>

   - Digital pipettors: Transfer a total of 1.60 mLs of sample into each dark cryovial
   - Transfer pipettes (disposable, plastic): one reference available to ensure filling the tubes with the proper volume:
   - Note the ridged pattern around the top part of the black cryovial. 1.6 mLs of liquid reaches the top of that pattern. See Figure 2 below.

Figure 2: Filling of Light Sensitive Dark Cryovials

e ridged
n the dark
1.6 mLs
the top of
l pattern.

New Barcode Label Identifiers



ntifier

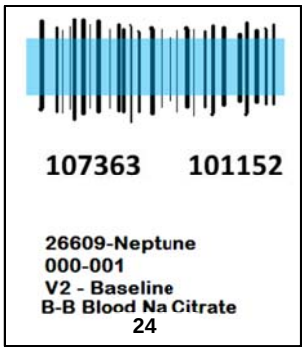
Participant Visit #

Sample Type

Aliquot Number
(this number is subject to change based on visit [Baseline/Follow-up] and participant weight)

26.A.2. BLOOD PROCESSING FOR SODIUM CITRATE (LIGHT BLUE TOP) TUBE 1

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **Baseline Visit [V2]** in the Sodium Citrate blood tube for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.



Required Supplies:
Included in kit:

- 1 x 4.5 mL Sodium Citrate blood vacutainer tubes[1] (Tube 1)
- 2 labeled cryovials[2] (**BLUE CAPS/BLUE LABELS)**
  (Both Pre-labeled with **B-B Blood Na Citra ##**

Provided by site:

- Blood sample from study participant
- Aerosol spray covers for centrifuge buckets
- Pipettors and tips or disposable pipettes (1 ml or 200 µl sizes) or plastic transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:

- Centrifuge capable of achieving 2000 x g (NOTE: G is not the same as RPM, please consult your centrifuge conversion table if necessary)
- University of Michigan OSEH[3] guidelines designate all work done with biological specimens that could produce spray from pipetting is done in a hood.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated alternate would provide this service.

Procedure
All baseline blood samples should be drawn prior to or within thirty days of the renal biopsy.

Note the date and start time of the blood draw (Tube 1) on Biospecimen Worksheet.
In accordance with the site's protocol for venipuncture, draw 1 (one) 4.5 mL Sodium Citrate blood vacutainers from adult participants. Following the blood draw the Research Coordinator will return to the lab with the samples.

1. Balance Sodium Citrate blood tube per your site's centrifuge protocol and handling policy.
2. Note the time on the Biospecimen worksheet (this should be the time the samples start to spin in the centrifuge).
3. Centrifuge the tube at 2000 x g for 12 minutes.

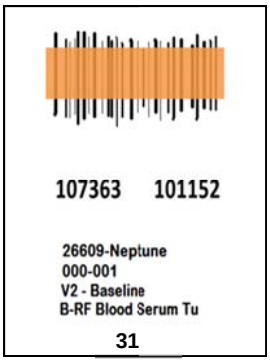
Sample processing:

4. After spinning, pipette plasma* from the Sodium Citrate tube into two equal aliquots of 1.6 mLs each (reference Figure 1 to determine proper volume). Use the cryovials labeled:
   B-B Blood Na Citrat ## and **B-B Blood Na Citrat ##**
5. Freeze aliquots at -80° C prior to shipping.
6. Discard remaining RBC's per OSEH guidelines

*Plasma is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance.

26.A.3. BLOOD PROCESSING FOR SERUM (BURNT ORANGE) TUBE 2

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **Baseline Visit [V2]** in the Serum blood tube for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.



Required Supplies:
Included in kit:

- 1 x 10.0 mL Serum blood vacutainer tube[4] wrapped in foil** (Tube 2)
- 3 labeled light sensitive Dark Cryovials[5] (**ORANGE LABELS**)
  (3 Pre-labeled **B-RF Blood Serum Tu ##**)

  ** *Sample must be protected from light (do **not** remove foil*)

Provided by site:

- Blood sample from study participant
- Aerosol spray covers for centrifuge buckets
- Pipettors and tips or disposable pipettes (1 ml or 200 µl sizes) or plastic transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:

- Centrifuge capable of achieving 2000 x g (NOTE: G is not the same as RPM, please consult your centrifuge conversion table if necessary)
- University of Michigan OSEH[3] guidelines designate all work done with biological specimens that could produce spray from pipetting is done in a hood.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated alternate would provide this service.

Procedure
All blood samples should be drawn prior to or within thirty days of the renal biopsy.

Note the date and start time of the blood draw (Tube 2) on Biospecimen Worksheet.
In accordance with the site's protocol for venipuncture, draw 1 (one) 10.0 mL Serum blood vacutainers from adult participants. Following the blood draw the Research Coordinator will return to the lab with the samples.

1. Balance Serum blood tube (tube 2) per your site's centrifuge protocol and handling policy.
2. Note the time on the Biospecimen worksheet (this should be the time the samples start to spin in the centrifuge).
3. Centrifuge the tube at 2000 x g for 12 minutes.

Sample processing:

4. After spinning, pipette serum*** from the tube into three aliquots of 1.60 mLs each (see Figure 2 to determine proper volume). Use the light-sensitive Dark cryovials labeled:

   B-RF Blood Serum Tu ## **B-RF Blood Serum Tu ##**
   B-RF Blood Serum Tu ##

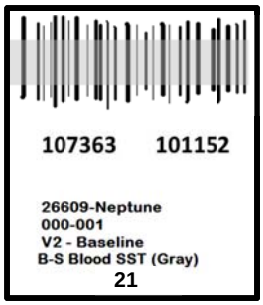
5. Freeze aliquots at -80° C prior to shipping.
6. Discard remaining RBC's per OSEH guidelines

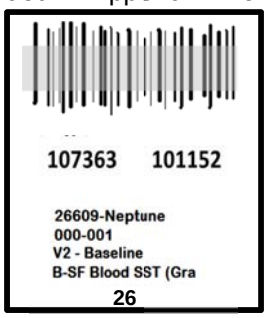
Procedure Class:	SPECIMENS
Procedure:	**BASELINE [V2] ADULT** BIO-Blood (BB, BRF, BS, BSF, BG, BE)

*** Serum is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance. Serum is not the same as plasma.

26.A.4. BLOOD PROCESSING FOR SST (RED/BLACK TIGER TOP) TUBES 3 and 4

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **Baseline Visit [V2]** in SST blood tubes for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.





Required Supplies:
Included in kit:

- 1 x 10.0 mL SST blood vacutainer tubes[6] (Tube 3)
- 3 labeled cryovials[2] (**GRAY CAPS/GRAY LABELS**)
  (Pre-labeled **B-S Blood SST (Gray ##**)

- 1 x 10.0 mL SST blood vacutainer tube[6] wrapped in foil** (Tube 4)
- 3 labeled light sensitive dark cryovials[5] (**Black, light prohibitive/ GREY LABELS**)
  (Pre-labeled **B-SF Blood SST (Gra ##)**

  ** *Sample must be protected from light (do **not** remove foil*)

Provided by site:

- Blood sample from study participant
- Aerosol spray covers for centrifuge buckets
- Pipettors and tips or disposable pipettes (1 ml or 200 µl sizes) or plastic transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:

- Centrifuge capable of achieving 2000 x g (NOTE: G is not the same as RPM, please consult your centrifuge conversion table if necessary)
- University of Michigan OSEH[3] guidelines designate all work done with biological specimens that could produce spray from pipetting is done in a hood.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated alternate would provide this service.

Procedure
All baseline blood samples should be drawn prior to or within thirty days of the renal biopsy.

At least one SST tube must be wrapped in aluminum foil *prior* to and following the blood draw, as well as while the sample is processed.

Note the date and start time of the blood draw (tubes 3-4) on Biospecimen Worksheet.

In accordance with the site's protocol for venipuncture, draw 2 (two) 10.0 mL SST blood vacutainers from adult participants. Following the blood draw the Research Coordinator will return to the lab with the samples.
The SST tubes must be processed following a 30-minute incubation period, placed in cryovials, and placed in the -80°C freezer.

Procedure Class:	SPECIMENS
Procedure:	**BASELINE [V2] ADULT** BIO-Blood (BB, BRF, BS, BSF, BG, BE)

Sample processing:

1. Following the 30-minute incubation period, balance SST blood tubes per your site's centrifuge protocol and handling policy.
2. Note the time on the Biospecimen worksheet (this should be the time the samples start to spin in the centrifuge).
3. Centrifuge SST tubes at 2000 x g for 12 minutes.

Tube 3

4. After spinning, remove tube from centrifuge keeping tubes upright so as not to disturb the serum*** component.
5. Pipette the serum layer from the un-foiled SST tubes (tube 3) into approximate 1.6 mL aliquots. This amount can be determined by referencing Figure 1. Use the cryovials labeled:

B-S Blood SST (Gray ## through **B-S Blood SST (Gray ##**

Tube 4

6. After spinning, pipette serum*** from the foiled SST tube (tube 4) into approximate 1.60 mL aliquots. This amount can be determined by referencing Figure 2. Use the light sensitive Dark cryovials labeled:

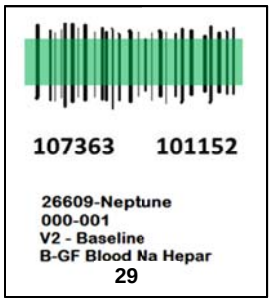
B-SF Blood SST (Gra ## through **B-SF Blood SST (Gra ##**

7. Freeze all aliquots at -80° C prior to shipping.
8. Discard remaining RBC's per OSEH guidelines

*** Serum is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance. Serum is not the same as plasma.

26.A.5. BLOOD PROCESSING FOR SODIUM HEPARIN (GREEN TOP) TUBE 5

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **Baseline Visit [V2]** in the Sodium Heparin blood tubes for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.



Required Supplies:
Included in kit:

- 1 x 4.0 mL Sodium Heparin blood vacutainer tube[7] wrapped in foil** (Tube 5)
- 2 labeled light sensitive dark cryovials[5] (**Black, light prohibitive/GREEN LABELS**) (Pre-labeled **B-GF Blood Na Hepar ##** and **B-GF Blood Na Hepar ##**)

*** Sample must be protected from light (do **not** remove foil*)

Provided by site:

- Blood sample from study participant
- Aerosol spray covers for centrifuge buckets
- Pipettes and tips or Disposable pipettes (1 ml or 200 µl sizes) or plastic Transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:

- Centrifuge capable of achieving 2000 x g (NOTE: G is not the same as RPM, please consult your centrifuge conversion table if necessary)
- University of Michigan OSEH[3] guidelines designate all work done with biological specimens that could produce spray from pipetting is done in a hood.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated alternate would provide this service.

Procedure
All baseline blood samples should be drawn prior to or within thirty days of the renal biopsy.

Note the date and start time of the blood draw (tube 5) on Biospecimen Worksheet.

In accordance with the site's protocol for venipuncture, draw 1 (one) 4.0 mL Sodium Citrate blood vacutainer (tube 5) from adult participants. Following the blood draw the Research Coordinator will return to the lab with the samples.

7. Balance Sodium Heparin blood tube (tube 6) per your site's centrifuge protocol and handling policy.
8. Note the time on the Biospecimen worksheet (this should be the time the samples start to spin in the centrifuge).
9. Centrifuge the tube at 2000 x g for 12 minutes.

Sample processing:

10. After spinning, pipette plasma* from the Sodium Heparin tube into two equal 1.60 mL aliquots, which can be determined using Figure 2. Use the two light sensitive Dark cryovials labeled:

B-GF Blood Na Hepar ## and **B-GF Blood Na Hepar ##**

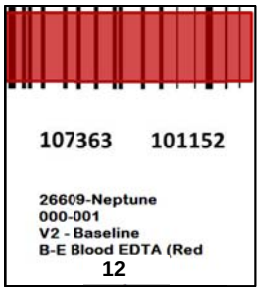
11. Freeze aliquots at -80° C prior to shipping.
12. Discard remaining RBC's per OSEH guidelines

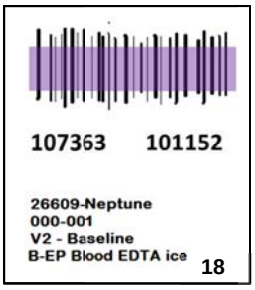
* Plasma is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance.

Procedure Class:	SPECIMENS
Procedure:	**BASELINE [V2] ADULT** BIO-Blood (BE, BS, BSF, BR, BB, BGF)

26.A.6. BLOOD PROCESSING FOR EDTA (PURPLE TOP) TUBES 6-11

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **Baseline Visit [V2]** in EDTA blood tubes for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.





Required Supplies:
Included in kit:

- 6 x 10.0 mL EDTA blood vacutainer tubes[8] (tubes 6-11)
- 17 labeled cryovials[2] (**RED CAPS/RED LABELS**)
  (Pre-labeled **B-E Blood EDTA (Red 1** through **B-E Blood EDTA (Red 17**)
- 3 labeled cryovials[2] (**PURPLE CAPS/PURPLE LABELS**)
  (Pre-labeled **B-EP Blood EDTA Ic 18** through **B-EP Blood EDTA Ic 20**)

Provided by site:

- Blood sample from study participant
- Aerosol spray covers for centrifuge buckets
- Pipettes and tips or Disposable pipettes (1 ml or 200 µl sizes) or plastic Transfer pipettes
- Gloves, goggles, and lab coat
- Ice and ice bucket

Required Equipment:

- Centrifuge capable of achieving 2000 x g (NOTE: G is not the same as RPM, please consult your centrifuge conversion table if necessary)
- University of Michigan OSEH[3] guidelines designate all work done with biological specimens that could produce spray from pipetting is done in a hood.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator the Site PI or designated alternate would provide this service.

Procedure
All blood samples should be drawn prior to or within thirty days of the renal biopsy visit [V3].

At least one EDTA tube must be on ice *prior* to the blood draw.

Note the date and start time of the blood draw (tubes 6-11) and fasting state on Biospecimen Worksheet.

In accordance with the site's protocol for venipuncture, draw 6 (six) 10.0 mL EDTA blood vacutainers from adult participants. The EDTA tubes must be PLACED ON ICE, processed, placed in cryovials, and placed in the -80°C freezer within 30 minutes. Following the blood draw the Research Coordinator will return to the lab with the samples.

Sample processing:

1. Balance EDTA blood tubes per site's centrifuge protocol and handling policy.
2. Note the time on the Biospecimen worksheet (this should be the time the samples start to spin in the centrifuge).
3. Centrifuge EDTA tubes at 2000 x g for 12 minutes.
4. Remove tubes from centrifuge keeping tubes upright so as not to disturb the plasma* component.

5. After spinning, pipette the plasma layer from all EDTA tubes into approximate 1.6 mL aliquots. This amount can be determined by referencing Figure 1. Use the cryovials labeled:

   B-E Blood EDTA (Red 1 through **B-E Blood EDTA (Red 17**

6. The EDTA tube which was "iced" prior to the blood draw and following should be spun as above.
7. After spinning, iced plasma should be put 1.6 mL aliquots into 3 cryovials labeled:
   B-EP Blood EDTA Ic 18 through **B-EP Blood EDTA Ic 20**
8. Freeze aliquots at -80° C prior to shipping.
9. Discard remaining RBC's per site's OSEH guidelines.

* Plasma is the top layer of the blood specimen after the centrifugation step. It should be a straw-colored yellow, semi-clear substance.

Procedure Class:	SPECIMENS
Procedure:	**BASELINE [V2] ADULT** BIO-Blood (BE, BS, BSF, BR, BB, BGF)

26.A.7. BLOOD PROCESSING FOR RNA PAXGENE (RED/CLEAR TOP) TUBE 12

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **Baseline Visit [V2]** in RNA PAXgene blood tubes for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Required Supplies:
Included in kit:

- 1 pre-labeled PAXgene RNA Blood Vacutainer[9] (**WHITE LABEL 'D RNA Paxgene (Whit'**) (Tube 12)

Provided by site:

- Blood sample from study participant
- Gloves, goggles, and lab coat

Required Equipment:

- No equipment is necessary for processing this specimen

Responsible Individuals
The Biobank Study Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Study Coordinator, the Biobank Lab Manager, followed by the Biobank Program Director/Site PI would serve as alternates.

Procedure
All blood samples should be drawn prior to renal biopsy, if biopsy is indicated. Following the biopsy, the Biobank Study Coordinator will return to the lab with the samples.

1. RNA blood vacutainer is marked with a **WHITE LABEL 'D RNA Paxgene (Whit'**
2. Blood draw:
   Summary:
   a. The PAXgene blood RNA vacutainer should be at room temperature prior to use.
   b. Fill the PAXgene RNA tube *after* all other tubes have been drawn.
   c. Collect blood into the PAXgene tube using your institution's recommended standard procedure for venipuncture.

   Blood Collection:
   a. Hold PAXgene tube vertically during blood draw, below point of venipuncture.
   b. Allow at least 10 seconds for complete blood draw; ensuring blood has stopped flowing into tube before removing from vacutainer holder.
   c. After blood collection gently invert tube 8-10 times.
   d. Store tube upright at room temperature for 2 hours.
   e. Following 2 hours room temperature incubation period, place in -80° C freezer upright.

Documentation
If PAXGene RNA tubes are left on shelf (room temp) for greater than 2 hour incubation period, please indicate additional elapsing time on the worksheet and case report forms. Additionally, if PAXgene RNA tubes stabilize at room temp for less than 2 hours, please indicate total time on worksheet and case report forms.

Procedure Class:	SPECIMENS
Procedure:	**BASELINE [V2] ADULT** BIO-Blood (BE, BS, BSF, BR, BB, BGF)

27.A.8. BLOOD PROCESSING FOR DNA PAXGENE (BLUE/CLEAR TOP) TUBE 13

Procedure Overview
This procedure describes the process for preparing blood samples obtained at the **Baseline Visit [V2]** in DNA PAXgene blood tubes for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Required Supplies:
Included in kit:

- 1 pre-labeled PAXgene DNA Blood Vacutainer[10] (BLUE LABEL 'C DNA Paxgene (Blue') (Tube 13)

Provided by site:
Blood sample from study participant

- Gloves, goggles, and lab coat

Required Equipment:

- No equipment is necessary for this specimen

Responsible Individuals
The Biobank Study Coordinator is responsible for retrieving blood samples from consented participants, returning sample to lab, and processing for storage. In the absence of the Study Coordinator, the Biobank Lab Manager, followed by the Biobank Program Director/Site PI would serve as alternates.

Procedure
All blood samples should be drawn prior to renal biopsy, if biopsy is indicated. Following the biopsy, the Biobank Study Coordinator will return to the lab with the samples.

3. DNA blood vacutainer is marked with a **BLUE LABEL 'C DNA Paxgene (Blue'**
4. Blood draw:
   Summary:
   a. The PAXgene blood DNA vacutainer should be at room temperature prior to use.
   b. Fill the PAXgene DNA tube *after* all other tubes have been drawn.
   c. Collect blood into the PAXgene tube using your institution's recommended standard procedure for venipuncture.

   Blood Collection:
   a. Hold PAXgene tube vertically during blood draw, below point of venipuncture.
   b. Allow at least 10 seconds for complete blood draw; ensuring blood has stopped flowing into tube before removing from vacutainer holder.
   c. After blood collection gently invert tube 8-10 times.
   d. Store tube upright at room temperature for 2 hours.
   e. Following 2 hours room temperature incubation period, please in -80° C freezer upright.

Documentation
If PAXgene DNA tubes are left on shelf (room temp) for greater than 2 hour incubation period, please indicate additional elapsing time on the worksheet and case report forms. Additionally, if PAXgene DNA tubes stabilize at room temp for less than 2 hours, please indicate total time on worksheet and case report forms.

All corresponding samples for each sample number should be stored together. If specimen does not adequately fill pre-determined number of aliquots, please document to minimize concerns regarding lost aliquots.

Complete the appropriate Biospecimen CRF corresponding to the study visit.

27.A.9. References

1. 4.5 mL Sodium Citrate Vacutainer: BD, Fisher Scientific ref No. 366415
2. Cryovials: DOT Scientific Inc. No. T334-6SPR
3. Check your local OSEH Guidelines
4. 10 mL Serum Vacutainer: BD, Fisher Scientific ref No. 366441
5. Light Sensitive Dark Cryovials: USA Scientific No. 1420-9709
6. 10 mL SST Vacutainer: BD, Fisher Scientific ref No. 367985
7. 4.0 mL Sodium Heparin Vacutainer: BD, Fisher Scientific ref No. 367871
8. 10 mL EDTA Vacutainer: BD, Fisher Scientific ref No. 366643
9. PreAnalytiX PAXgene Blood RNA Tube; 2.5 mL Vacutainer: ref. No. 762165
   http://www.preanalytix.com/product-catalog/blood/rna/products/paxgene-blood-rna-tube/
10. PreAnalytiX PAXgene DNA Tube; 8.5 mL Vacutainer: Cat. No. 761115
    http://www.preanalytix.com/DNA.asp
11. See attached MSDS for relevant safety precautions and hazards.

Centrifugation steps were performed in a SORVALL Legend T with radius 15.9 cm. If alternate centrifuges are used, the following equation may be used to calculate appropriate RPM necessary to generate the G-force indicated in above protocol:

$$RCF = 11.18 * \left(\frac{n}{1000}\right)^2 * r$$

RCF = Relative Centrifugal Force (G); a dimensionless number allowing comparison of separation efficiency

r = radius of centrifugation in cm

n = speed in rpm

Procedure Class:	SPECIMENS
Procedure:	**BASELINE [V2] ADULT** BIO-Blood (BE, BS, BSF, BR, BB, BGF)

110 cc Adult Baseline Blood Draw

Tube #	Tube Type	Step 1	Step 2	Step 3	Step 4	Step 5
1	4.5 mL Sodium Citrate	Process within one hour.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL aliquots of serum into 2 cryovials	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
2	10 mL Serum Wrapped in Foil	Avoid exposure to light. Allow to clot for 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.60 mL aliquots of serum into 3 light sensitive Dark cryovials	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
3	10 mL SST	Allow to clot for 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 3 cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
4	10 mL SST Wrapped in Foil	Avoid exposure to light. Allow to clot for 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.60 mL aliquots of serum into 3 light sensitive Dark cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
5	4 mL Sodium Heparin Wrapped in Foil	Avoid exposure to light.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.60 ml aliquots of serum to 2 light sensitive Dark cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
6	10 mL EDTA	Keep on ice. Process within 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 3 cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
7	10 mL EDTA	Keep on ice. Process within 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 3 cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
8	10 mL EDTA	Keep on ice. Process within 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 3 cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
9	10 mL EDTA	Keep on ice. Process within 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 3 cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
10	10 mL EDTA	Keep on ice. Process within 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 3 cryovials..	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
11	10 mL EDTA	Keep on ice. Process within 30 minutes.	Centrifuge for 12 minutes at 2000 x G	Transfer 1.6 mL of serum into 3 cryovials.	Store aliquots at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
12	2.5 mL RNA	Must sit at room temp for 2 hours	Freeze at -80		Store pre-labeled vacutainer at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule
13	8.5 mL DNA	Must sit at room temp for 2 hours	Freeze at -80		Store pre-labeled vacutainer at -80°C	Ship to NEPTUNE Biobank as indicated by site schedule

* approximate

Adult Blood Draw Guide

Tube #	Tube Type	Adults	
		Baseline [V2]	Follow-Up [V4-V13]
1	4.5 mL Na Citrate	4.5	4.5
	Cryovials:	*2: **blue** caps*	
2	10 mL Serum - Foil	10	
16	3 mL Serum - Foil		3
	Light Sensitive Cryovials:	*3 – **Orange** Cap*	*1 – **Orange** Cap*
3	10 mL SST	10	10
	Cryovials:	*3- Grey Caps*	
4	10 mL SST - Foil	10	
17	3.5 mL SST - Foil		3.5
	Light Sensitive Cryovials:	*3 – Grey Caps*	*1 – Grey Cap*
5	4 mL Na Heparin- Foil	4	
18	2 mL Na Heparin- Foil		2
	Light Sensitive Cryovials:	*2 – **Green** Caps*	*1 – **Green** Cap*
6	10 mL EDTA	10	10
7	10 mL EDTA	10	10
8	10 mL EDTA	10	10
9	10 mL EDTA	10	*10 (iced)
10	10 mL EDTA	10	
11	10 mL EDTA	*10 (iced)	
14	4 mL EDTA (*Iced for peds >21 lbs)		
15	6 mL EDTA		
	Cryovials:	*17- **Red** Caps* **3 – **Purple***	*11- **Red** Caps* **3 – **Purple***
12	2.5 mL RNA PAXGene	2.5	2.5
13	8.5 mL DNA PAXGene	8.5	
Blood Draw Totals (mLs)		**110**	**65.5**

26.A.11. Pediatric Blood Draw Guide

Tube #	Tube Type	< 21 pounds	21-51 pounds	≥ 52 pounds	
		Baseline[V2] & Follow-Up [V4-V13}	Baseline[V2] & Follow-Up [V4-V13]	Baseline [V2]	Follow-Up [V4-V13]
1	4.5 mL Na Citrate		4.5	4.5	4.5
	Cryovials:		*2: **blue** caps*	*2: **blue** caps*	
2	10 mL Serum - Foil		10	10	10
16	3 mL Serum - Foil	3			
	Light Sensitive Cryovials:	*1 – **Orange** Cap*	*3 – **Orange** Caps*	*3 – **Orange** Caps*	
3	10 mL SST			10	10
	Cryovials:			*3- Grey Caps*	
4	10 mL SST - Foil		10	10	10
17	3.5 mL SST - Foil	3.5			
	Light Sensitive Cryovials:	*1 – Grey Cap*	*3 – Grey Caps*	*3 – Grey Caps*	
5	4 mL Na Heparin- Foil		4	4	4
18	2 mL Na Heparin- Foil	2			
	Light Sensitive Cryovials:	*1 – **Green** Cap*	*2 – **Green** Caps*	*2 – **Green** Caps*	
6	10 mL EDTA		10	10	10
7	10 mL EDTA			10	10
8	10 mL EDTA			10	
9	10 mL EDTA			10	
14	4 mL EDTA (*Iced for peds >21 lbs)	4	*4	*4	*4
15	6 mL EDTA	5	5	6	
	Cryovials:	*3 – **Red** Caps*	*5 – **Red** Caps,*	*14 – **Red** Caps* **2 – **Purple***	*6- **Red** Caps* **2 – **Purple***
12	2.5 mL RNA PAXGene	2.5	2.5	2.5	2.5
13	8.5 mL DNA PAXGene			8.5	
Blood Draw Totals (mLs)		**20**	**50**	**99.5**	**65**

The DNA tube should only be obtained one time over the course of the study. Once the DNA draw is complete, the subsequent visits please supplement the 8.5 mL DNA draw with a complete 10 mL EDTA tube draw. (This applies for the 21-51 pound participant follow-up visits)

Procedure Class:	SPECIMENS
Procedure:	BIO-Spot Urine (SU, AS, AQ and AP)

26.B.1. UPDATES TO SPOT URINE PROCESSING PROCEDURES:

Effective 11/2012

1. Research Coordinators (RCs) will no longer fill sets of cryovials with equal volumes of sample. Effective 11/2012 please fill each cryovial with the maximum volume (1.6 mL) in sequential order (based on the aliquot number indicated on barcoded label) until all corresponding urine sample has been aliquotted. Discard remaining empty cryovials on-site.

2. When transferring urine from the original collection container or the processing tube for freezer storage, it is imperative that these containers are not overfilled. The following procedures take into account liquid expansion when samples freeze.

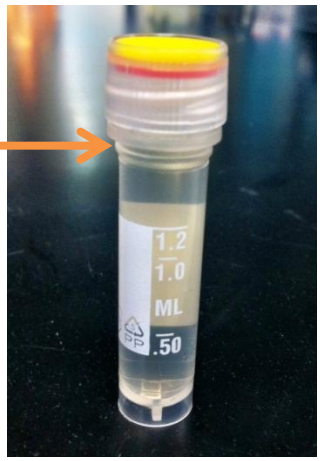
   a) Filling cryovials with biospecimens:

   - Digital pipettors: Transfer a total of 1.6 mls of sample into the cryovials.
   - Transfer pipettes (disposable, plastic): Note the two ridges below the cap of the cryovial. Use the lower ridge as a reference point for filling cryovials. Please see Figure 1 below.

When transferring urine samples from the centrifuge tubes into cryovials for freezer storage, it is imperative that these containers are not overfilled. The following directions take into account urine volume expansion when frozen.

Figure 1: Filling of Cryovials

The small, lowest ridge on the cryovial should be used for reference. Fill cryovial to this point, or with 1.6 mLs of sample.



Procedure Class:	SPECIMENS
Procedure:	BIO-Spot Urine (SU, AS, AQ and AP)

26.B.2. Spot/Random Clean Catch Urine Specimen Processing Procedure

Procedure Overview

This procedure describes the process for preparing one whole urine sample type (U), two urine supernatant sample types (S, Q) and 2 urine pellet sample types(AP-E and AP-Q) from a spot (random) urine sample for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

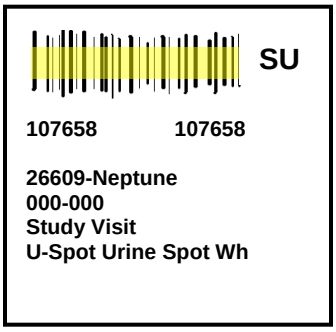
Spot urine is collected in the same fashion for both pediatric and adult study participants. Spot urine samples are obtained at each study visit, including the baseline [V2] and the Biopsy [V3] visits, and all follow-up visits.

Required Supplies:
Included in kit:

- 2 x 15.0 mL centrifuge tubes[1] empty (marked **"EMPTY"**)
- 2 x 15.0 mL centrifuge tubes containing 15 μL of Protease Inhibitor[2] (marked **"PI"**)
- 16 x 1.8 mL cryovials[3] with yellow caps
  (Pre-labeled as follows)

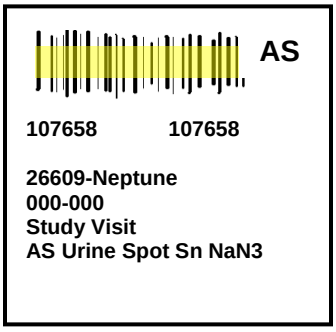
Sample 1:
SU = Whole, Unprocessed Urine

4 pre-labeled, empty cryovials
U-Spot Urine Spot Wh



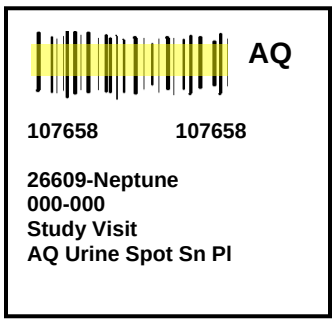
Sample 2:
AS = Processed & NaAzide

4 pre-labeled cryovials containing Sodium Azide[4]
AS Urine Spot SN NaN3



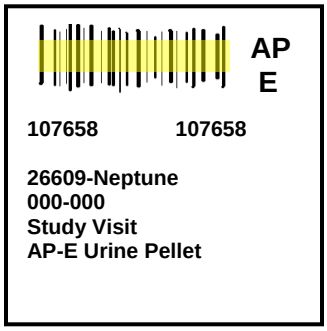
Sample 3:
AQ = Processed & Protease Inhibitor (PI)

4 pre-labeled cryovials for Protease Inhibitor
AQ Urine Spot SN PI



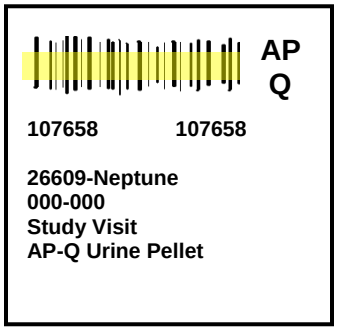
Sample 4:
AP-E = Urine Pellet from 'Empty' centrifuge tubes

2 pre-labeled, empty cryovials
AP-E Urine Pellet



Sample 5:
AP-Q = Urine Pellet from 'PI' containing centrifuge tubes

2 pre-labeled, empty cryovials
AP-Q Urine Pellet



- RNA-Later[5] (expected use per sample: 50-100 μL)

Provided by site:
- Spot Urine sample from study participant
- Pipettes and tips or disposable pipettes (10 ml, 5 ml, 1 ml sizes) or plastic Transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:
- Centrifuge capable of achieving 2000 x G
- University of Michigan OSEH guidelines designate all work done with biological specimens that could produce spray from pipetting be done in a hood. Please refer to your site specific OSEH policies.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving urine sample from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated, NEPTUNE trained alternate would provide this service.

Procedure:
1. Midstream urine is recovered in sterile specimen container and stored on ice. A minimum of 32 mL of urine is necessary.
2. Note time, fasting state and 1st, 2nd, 3rd, etc urine of the day on study visit worksheet (if patient is able to provide this detail, otherwise, indicate "No recall").

Procedure Class:	SPECIMENS
Procedure:	BIO-Spot Urine (SU, AS, AQ and AP)

If processing is not able to be completed immediately, please store on ice or refrigerate for a maximum of 4 hours.

Sample processing:

Sample 1

*Requires total spot urine sample of 60 mL minimum; if sample is 50 mL or less please note in worksheet and CRF and do NOT store spot urine for the U-Spot Samples: * NO WHOLE URINE SAMPLE**

3. Using a pipettor, transfer ***whole***, unprocessed urine into the cryovials labeled:

'SU' to the right of the barcode

4. Replace the cap, firmly twisting in a clockwise direction.

Samples 2 & 3

5. Pour the remaining urine into the 4 x 15.0 mL centrifuge tubes in equal 12 milliliter portions (two tubes of each marked "EMPTY" and "Protease Inhibitor (PI)")

   E.g.:

   30 mL of spot urine → 2 – 12.0 mL centrifuge tubes for spinning (Use 1 'Empty' and 1 'PI' tube)

   50 mL of urine → 4 – 12.0 mL centrifuge tube; discard remaining urine (Use 2 of each, 'Empty' and 'PI')

NOTE: Use at least ONE EACH: "EMPTY" and "PI" centrifuge tubes

6. In the tubes labeled "PI", gently invert 8-10 times to dissolve the PI completely. Remove the cap to allow any air bubbles to escape, replace cap tightly.
7. Spin all 4 tubes at 1000 X G for 12 minutes in centrifuge

Sample 2 (AS Urine Spot): From the tubes labeled "EMPTY", transfer urine using a transfer pipettor into the 4 cryovials containing a pre-measured amount of 100 mM Sodium Azide (a biocide) labeled:

'AS' to the right of the barcode

8. When opening each cryovial, take care to place the cap directly in front of the respective tube to retain pre-measured volumes for consistent concentrations in each aliquot.
9. Pipette 1.6 mLs of urine or enough urine to fill the cryovial up to the first ridge on the cryovial (see Figure 1).
10. Replace the cap, firmly twisting in a clockwise direction. After all caps are replaced, invert tubes *at least 2 times* to distribute the sodium azide prior to freezing.

Sample 3 (AQ Urine Spot): From the tubes labeled "PI", transfer urine using a transfer pipettor into the cryovials labeled:

'AQ' to the right of the barcode

11. Pipette 1.6 mLs of urine or enough urine to fill the cryovial up to the first ridge on the cryovial (see Figure 1).

Samples 4 and 5

12. Pour off remaining supernatant from all of the 15.0 mL centrifuge tubes

13. For maximal drainage, gently invert centrifuge tubes on clean paper towels for 10 seconds, take care to not disturb pellet in the centrifuge tube tip.
14. With a clean pipette tip, transfer 25.0-50.0* μL RNA-Later into each centrifuge tube, take care to not touch the inside walls of the centrifuge tube.
15. Gently stir the mixture with the pipette tip, changing tips when moving between the 'Empty' tubes and the 'PI' tubes. **Do not pipette up and down to mix as this could break any cells present in the pellet.**

    Sample 4 (AP-E Urine Pellet): From the centrifuge tubes labeled "EMPTY", pipette one urine pellet from each centrifuge tube into the two cryovials labeled:

    'AP-E' to the right of the barcode

    Sample 5 (AP-Q Urine Pellet): From the centrifuge tubes labeled "PI", pipette one urine pellet from each centrifuge tube into the two cryovials labeled:

    'AP-Q' to the right of the barcode

16. Freeze all samples at -80 C.
17. Residual urine may be disposed per OSEH guidelines enforced at participating institution.

* Amount of RNA-Later will vary depending on size of pellet. RNA-Later should be added to completely submerse the pellet.

Shipping
Samples should be shipped according to the site-specific scheduled interval for shipments.

All specimens should be shipped together **on dry ice** using the shipping instructions found in Appendix N and in the study specific container provided by NEPTUNE.

Documentation
All corresponding samples for each participant ID should be stored together. If specimen does not adequately fill pre-determined number of aliquots, please document to minimize concerns regarding lost aliquots.

Complete the appropriate Biospecimen CRF corresponding to the study visit.

26.B.3. References

1. 15.0 mL orange-capped Corning centrifuge tubes: Fisher Scientific No. 05-538-53D, Corning No. 430052
2. Protease Inhibitor Cocktail: Sigma-Aldrich Catalog: P1860 – 1 mL
3. Cryovials: DOT Scientific Inc. No.: T334-6SPR
4. Sodium Azide (see attached MSDS)
5. Ambion RNA-Later Solution; P/N: Am7021
6. University of Michigan Occupations Safety and Environmental Health (OSEH) guidelines indicate washing urine and its debris down laboratory sink with adequate water.

Relevant Definitions: NaN_3: Sodium Azide

SIGMA-ALDRICH

sigma-aldrich.com

Material Safety Data Sheet

Version 4.1
Revision Date 01/19/2012
Print Date 11/29/2012

1. PRODUCT AND COMPANY IDENTIFICATION

Product name	:	Protease Inhibitor Cocktail
Product Number	:	P1860
Brand	:	Sigma
Supplier	:	Sigma-Aldrich 3050 Spruce Street SAINT LOUIS MO 63103 USA
Telephone	:	+1 800-325-5832
Fax	:	+1 800-325-5052
Emergency Phone # (For both supplier and manufacturer)	:	(314) 776-6555
Preparation Information	:	Sigma-Aldrich Corporation Product Safety - Americas Region 1-800-521-8956

2. HAZARDS IDENTIFICATION

Emergency Overview

OSHA Hazards
Combustible Liquid, Target Organ Effect

Target Organs

Eyes, Skin

GHS Classification
Flammable liquids (Category 4)

GHS Label elements, including precautionary statements

Pictogram	none
Signal word	Warning
Hazard statement(s)	
H227	Combustible liquid
Precautionary statement(s)	none

HMIS Classification

Health hazard:	0
Chronic Health Hazard:	*
Flammability:	2
Physical hazards:	0

NFPA Rating

Health hazard:	0
Fire:	2
Reactivity Hazard:	0

Potential Health Effects

Inhalation	May be harmful if inhaled. Causes respiratory tract irritation.
Skin	May be harmful if absorbed through skin. Causes skin irritation.

Eyes	Causes eye irritation.
Ingestion	May be harmful if swallowed.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Component		Classification	Concentration
Dimethyl sulfoxide			
CAS-No. EC-No.	67-68-5 200-664-3		60 - 100 %

4. FIRST AID MEASURES

General advice
Consult a physician. Show this safety data sheet to the doctor in attendance.Move out of dangerous area.

If inhaled
If breathed in, move person into fresh air. If not breathing, give artificial respiration. Consult a physician.

In case of skin contact
Wash off with soap and plenty of water. Consult a physician.

In case of eye contact
Rinse thoroughly with plenty of water for at least 15 minutes and consult a physician.

If swallowed
Do NOT induce vomiting. Never give anything by mouth to an unconscious person. Rinse mouth with water. Consult a physician.

5. FIREFIGHTING MEASURES

Suitable extinguishing media
For small (incipient) fires, use media such as "alcohol" foam, dry chemical, or carbon dioxide. For large fires, apply water from as far as possible. Use very large quantities (flooding) of water applied as a mist or spray; solid streams of water may be ineffective. Cool all affected containers with flooding quantities of water.

Special protective equipment for firefighters
Wear self contained breathing apparatus for fire fighting if necessary.

Hazardous combustion products
Hazardous decomposition products formed under fire conditions. - Carbon oxides, Sulphur oxides

Further information
Use water spray to cool unopened containers.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions
Use personal protective equipment. Avoid breathing vapors, mist or gas. Ensure adequate ventilation. Remove all sources of ignition. Beware of vapours accumulating to form explosive concentrations. Vapours can accumulate in low areas.

Environmental precautions
Prevent further leakage or spillage if safe to do so. Do not let product enter drains.

Methods and materials for containment and cleaning up
Contain spillage, and then collect with an electrically protected vacuum cleaner or by wet-brushing and place in container for disposal according to local regulations (see section 13). Keep in suitable, closed containers for disposal.

7. HANDLING AND STORAGE

Precautions for safe handling
Avoid contact with skin and eyes. Avoid inhalation of vapour or mist.
Keep away from sources of ignition - No smoking. Take measures to prevent the build up of electrostatic charge.

Conditions for safe storage
Keep container tightly closed in a dry and well-ventilated place.

Recommended storage temperature: -20 °C

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

Components	CAS-No.	Value	Control parameters	Basis
Dimethyl sulfoxide	67-68-5	TWA	250 ppm	USA. Workplace Environmental Exposure Levels (WEEL)

Personal protective equipment

Respiratory protection
Where risk assessment shows air-purifying respirators are appropriate use a full-face respirator with multi-purpose combination (US) or type ABEK (EN 14387) respirator cartridges as a backup to engineering controls. If the respirator is the sole means of protection, use a full-face supplied air respirator. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU).

Hand protection
Handle with gloves. Gloves must be inspected prior to use. Use proper glove removal technique (without touching glove's outer surface) to avoid skin contact with this product. Dispose of contaminated gloves after use in accordance with applicable laws and good laboratory practices. Wash and dry hands.

Eye protection
Safety glasses with side-shields conforming to EN166 Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN 166(EU).

Skin and body protection
impervious clothing, The type of protective equipment must be selected according to the concentration and amount of the dangerous substance at the specific workplace.

Hygiene measures
Handle in accordance with good industrial hygiene and safety practice. Wash hands before breaks and at the end of workday.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance

Form	liquid
Colour	no data available

Safety data

pH	no data available
Melting point/freezing point	no data available
Boiling point	no data available
Flash point	87 °C (189 °F)
Ignition temperature	no data available
Autoignition temperature	no data available
Lower explosion limit	no data available
Upper explosion limit	no data available
Vapour pressure	no data available
Density	no data available
Water solubility	no data available
Partition coefficient:	no data available

n-octanol/water	
Relative vapour density	no data available
Odour	no data available
Odour Threshold	no data available
Evaporation rate	no data available

10. STABILITY AND REACTIVITY

Chemical stability
Stable under recommended storage conditions.

Possibility of hazardous reactions
no data available

Conditions to avoid
Heat, flames and sparks.

Materials to avoid
no data available

Hazardous decomposition products
Hazardous decomposition products formed under fire conditions. - Carbon oxides, Sulphur oxides
Other decomposition products - no data available

11. TOXICOLOGICAL INFORMATION

Acute toxicity

Oral LD50
no data available

Inhalation LC50
no data available

Dermal LD50
no data available

Other information on acute toxicity
no data available

Skin corrosion/irritation
no data available

Serious eye damage/eye irritation
Eyes: no data available

Respiratory or skin sensitization
no data available

Germ cell mutagenicity

no data available

Carcinogenicity

IARC:	No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.
ACGIH:	No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by ACGIH.
NTP:	No component of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.
OSHA:	No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by OSHA.

Reproductive toxicity

no data available

Teratogenicity

no data available

Specific target organ toxicity - single exposure (Globally Harmonized System)
no data available

Specific target organ toxicity - repeated exposure (Globally Harmonized System)
no data available

Aspiration hazard
no data available

Potential health effects

Inhalation	May be harmful if inhaled. Causes respiratory tract irritation.
Ingestion	May be harmful if swallowed.
Skin	May be harmful if absorbed through skin. Causes skin irritation.
Eyes	Causes eye irritation.

Synergistic effects
no data available

Additional Information
RTECS: Not available

12. ECOLOGICAL INFORMATION

Toxicity

no data available

Persistence and degradability
no data available

Bioaccumulative potential
no data available

Mobility in soil
no data available

PBT and vPvB assessment
no data available

Other adverse effects

no data available

13. DISPOSAL CONSIDERATIONS

Product
This combustible material may be burned in a chemical incinerator equipped with an afterburner and scrubber. Offer surplus and non-recyclable solutions to a licensed disposal company. Contact a licensed professional waste disposal service to dispose of this material.

Contaminated packaging
Dispose of as unused product.

14. TRANSPORT INFORMATION

DOT (US)

NA-Number: 1993 Class: CBL Packing group: III
Proper shipping name: Combustible liquid, n.o.s. (Dimethyl sulfoxide)
Marine pollutant: No
Poison Inhalation Hazard: No

IMDG
Not dangerous goods

IATA
Not dangerous goods

15. REGULATORY INFORMATION

OSHA Hazards
Combustible Liquid, Target Organ Effect

SARA 302 Components
SARA 302: No chemicals in this material are subject to the reporting requirements of SARA Title III, Section 302.

SARA 313 Components
SARA 313: This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

SARA 311/312 Hazards
Fire Hazard, Chronic Health Hazard

Massachusetts Right To Know Components
No components are subject to the Massachusetts Right to Know Act.

Pennsylvania Right To Know Components

	CAS-No.	Revision Date
Dimethyl sulfoxide	67-68-5	2007-03-01

New Jersey Right To Know Components

	CAS-No.	Revision Date
Dimethyl sulfoxide	67-68-5	2007-03-01

California Prop. 65 Components
This product does not contain any chemicals known to State of California to cause cancer, birth defects, or any other reproductive harm.

16. OTHER INFORMATION

Further information

The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. It does not represent any guarantee of the properties of the product. Sigma-Aldrich Corporation and its Affiliates shall not be held liable for any damage resulting from handling or from contact with the above product. See www.sigma-aldrich.com and/or the reverse side of invoice or packing slip for additional terms and conditions of sale.

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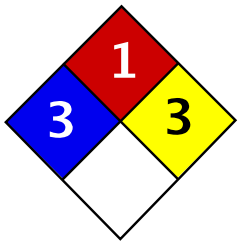

Health	3
Fire	1
Reactivity	3
Personal Protection	E

Material Safety Data Sheet
Sodium azide MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium azide

Catalog Codes: SLS1363

CAS#: 26628-22-8

RTECS: VY8050000

TSCA: TSCA 8(b) inventory: Sodium azide

CI#: Not available.

Synonym:

Chemical Name: Hydrazoic Acid, Sodium Salt

Chemical Formula: NaN3

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium azide	26628-22-8	100

Toxicological Data on Ingredients: Sodium azide: ORAL (LD50): Acute: 27 mg/kg [Rat]. 27 mg/kg [Mouse]. DERMAL (LD50): Acute: 20 mg/kg [Rabbit].

Section 3: Hazards Identification

Potential Acute Health Effects:
Very hazardous in case of skin contact (irritant), of eye contact (irritant). Hazardous in case of ingestion, of inhalation. Slightly hazardous in case of skin contact (permeator). Severe over-exposure can result in death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:
CARCINOGENIC EFFECTS: Not available.
MUTAGENIC EFFECTS: Not available.
TERATOGENIC EFFECTS: Not available.
DEVELOPMENTAL TOXICITY: Not available.
Repeated exposure to an highly toxic material may produce general deterioration of health by an accumulation in one or many human organs.

Section 4: First Aid Measures

Eye Contact:
Check for and remove any contact lenses. Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. Cold water may be used. Do not use an eye ointment. Seek medical attention.

Skin Contact:
After contact with skin, wash immediately with plenty of water. Gently and thoroughly wash the contaminated skin with running water and non-abrasive soap. Be particularly careful to clean folds, crevices, creases and groin. Cold water may be used. Cover the irritated skin with an emollient. If irritation persists, seek medical attention. Wash contaminated clothing before reusing.

Serious Skin Contact:
Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.

Inhalation: Allow the victim to rest in a well ventilated area. Seek immediate medical attention.

Serious Inhalation:
Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek medical attention.

Ingestion:
Do not induce vomiting. Examine the lips and mouth to ascertain whether the tissues are damaged, a possible indication that the toxic material was ingested; the absence of such signs, however, is not conclusive. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: Not available.

Flammable Limits: Not available.

Products of Combustion: Some metallic oxides.

Fire Hazards in Presence of Various Substances: Highly flammable in presence of shocks.

Explosion Hazards in Presence of Various Substances:
Risks of explosion of the product in presence of static discharge: Not available.
Highly explosive in presence of shocks, of metals.

Fire Fighting Media and Instructions:
SMALL FIRE: Use DRY chemical powder.
LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill: Use appropriate tools to put the spilled solid in a convenient waste disposal container.

Large Spill:
Use a shovel to put the material into a convenient waste disposal container. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:
Keep locked up Keep away from heat. Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the residue under a fume hood. Ground all equipment containing material. Do not ingest. Do not breathe dust. Take precautionary measures against electrostatic discharges. In case of insufficient ventilation, wear suitable respiratory equipment If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes Keep away from incompatibles such as metals.

Storage:
Keep container dry. Keep in a cool place. Ground all equipment containing material. Keep container tightly closed. Keep in a cool, well-ventilated place. Highly toxic or infectious materials should be stored in a separate locked safety storage cabinet or room.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:
Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection:
Splash goggles. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:
Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: TWA: 0.29 (mg/m3) from ACGIHConsult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid.

Odor: Not available.

Taste: Not available.

Molecular Weight: 65.02 g/mole

Color: Not available.

pH (1% soln/water): Not available.

Boiling Point: Not available.

Melting Point: Decomposes.

Critical Temperature: Not available.

Specific Gravity: 1.846 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility: Soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: Unstable.

Instability Temperature: Not available.

Conditions of Instability: Not available.

Incompatibility with various substances: Extremely reactive or incompatible with metals.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: No.

Section 11: Toxicological Information

Routes of Entry: Eye contact. Inhalation. Ingestion.

Toxicity to Animals:
Acute oral toxicity (LD50): 27 mg/kg [Mouse].
Acute dermal toxicity (LD50): 20 mg/kg [Rabbit].

Chronic Effects on Humans: Not available.

Other Toxic Effects on Humans:
Very hazardous in case of skin contact (irritant).
Hazardous in case of ingestion, of inhalation.
Slightly hazardous in case of skin contact (permeator).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans: Not available.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation: Possibly hazardous short/long term degradation products are to be expected.

Toxicity of the Products of Biodegradation: The products of degradation are more toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Section 14: Transport Information

DOT Classification: CLASS 6.1: Poisonous material.

Identification: : Sodium azide : UN1867 PG: II

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:
Pennsylvania RTK: Sodium azide
Massachusetts RTK: Sodium azide
TSCA 8(b) inventory: Sodium azide
SARA 302/304/311/312 extremely hazardous substances: Sodium azide
SARA 313 toxic chemical notification and release reporting: Sodium azide
CERCLA: Hazardous substances.: Sodium azide

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada): CLASS D-1A: Material causing immediate and serious toxic effects (VERY TOXIC).

DSCL (EEC):
R38- Irritating to skin.
R41- Risk of serious damage to eyes.

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 1

Reactivity: 3

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 1

Reactivity: 3

Specific hazard:

Protective Equipment:
Gloves.
Lab coat.
Dust respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.
Splash goggles.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

Created: 10/11/2005 12:32 PM

Last Updated: 11/06/2008 12:00 PM

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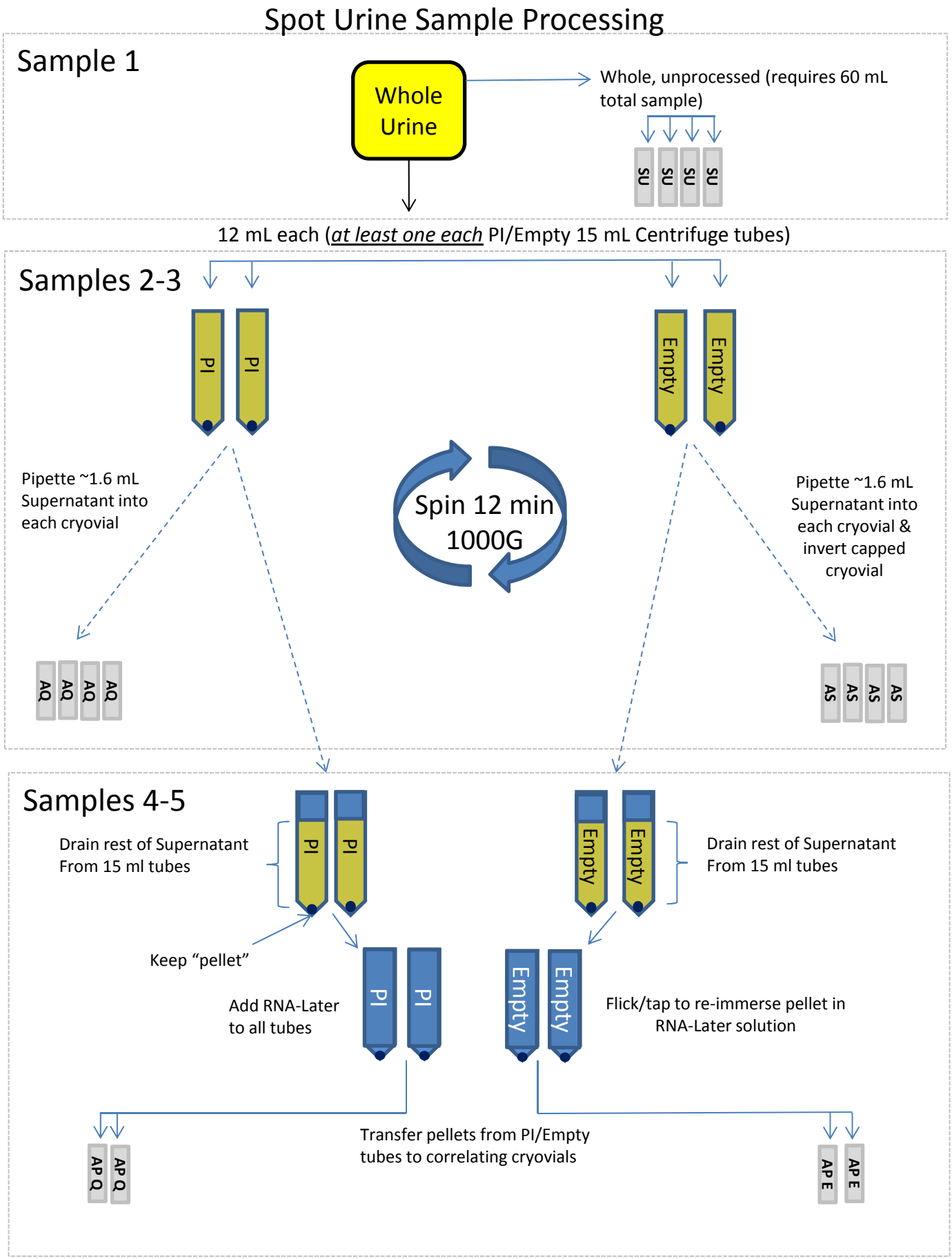

Spot Urine Sample Processing
Sample 1
Whole Urine
Whole, unprocessed (requires 60 mL total sample)
SU
SU
SU
SU
12 mL each (at least one each PI/Empty 15 mL Centrifuge tubes)
Samples 2-3
PI
PI
Empty
Empty
Pipette ~1.6 mL Supernatant into each cryovial
Spin 12 min 1000G
Pipette ~1.6 mL Supernatant into each cryovial & invert capped cryovial
AQ
AQ
AQ
AQ
AS
AS
AS
AS
Samples 4-5
Drain rest of Supernatant From 15 ml tubes
PI
PI
Empty
Empty
Drain rest of Supernatant From 15 ml tubes
Keep "pellet"
Add RNA-Later to all tubes
PI
PI
Empty
Empty
Flick/tap to re-immerse pellet in RNA-Later solution
Transfer pellets from PI/Empty tubes to correlating cryovials
AP Q
AP Q
AP E
AP E

Procedure Class:	SPECIMENS
Procedure:	BIO-24-Urine (U, UQ)

26.C.1. UPDATES TO 24-HOUR URINE SAMPLE PROCESSING PROCEDURES

Effective 11/2012

1. Research Coordinators (RCs) will no longer fill sets of centrifuge tubes or cryovials with equal volumes of sample. Effective 11/2012 please fill each tube/cryovial with the maximum volume (40.0 mL and 4.5 mL, respectively) in sequential order (based on the aliquot number indicated on barcoded label) until all corresponding urine sample has been aliquotted. Discard remaining empty cryovials on-site.

2. When transferring urine from the original collection container or the processing tube for freezer storage, it is imperative that these containers are not overfilled. The following procedures take into account liquid expansion when samples freeze.

   When transferring 24-hour samples into the 50 and 5 mL storage tubes, it is imperative that the tubes are not overfilled. The following directions take into account urine volume expansion when frozen.

   a) 50 mL centrifuge tubes: Do not fill beyond 40 mLs of urine (Figure 1)
   b) 5 ml cryovials: Do not fill beyond 4.5 mls of urine (Figure 2)

(Please references the images below)

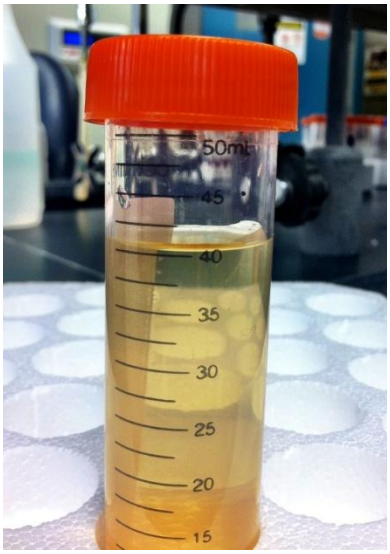


Figure 1: 50 mL centrifuge tube
Filled properly with 40 mLs of urine

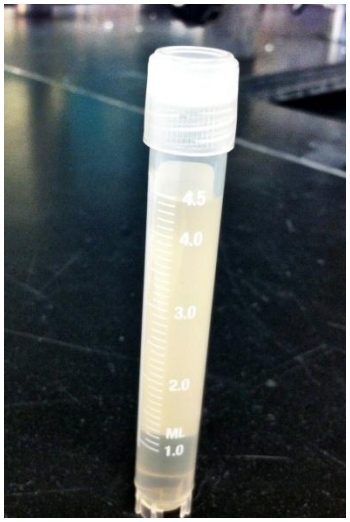


Figure 2: 5.0 mL cryovial
Filled properly with 4.5 mLs of urine

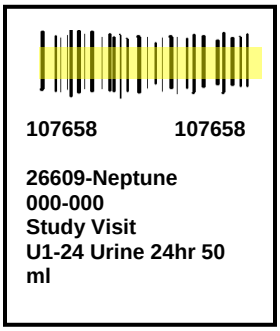
Procedure Class:	SPECIMENS
Procedure:	BIO-24-Urine (U, UQ)

26.C.2. 24-Hour or Timed Urine Processing Procedure

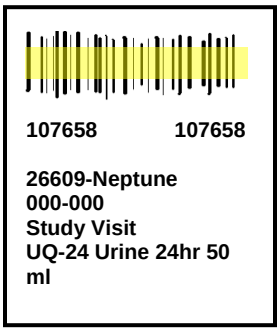
Procedure Overview
This procedure describes the process for preparing aliquots of the 24-hour urine sample for NEPTUNE storage at -80° C. Shipping details are provided in Appendix N of the NEPTUNE Manual of Procedures.

Required Supplies:
Included in kit:

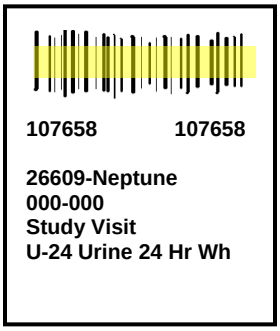
- 2 x 50 mL orange top centrifuge tubes
- 5 x 5.0 mL cryovials
  (Pre-labeled as follows)
- 1 pre-labeled, empty 50 mL centrifuge tube[1] labeled as follows:



- 1 pre-labeled, 50 mL centrifuge tube containing 6 μL of Protease Inhibitor[2]



- 5 pre-labeled 5.0 mL cryovials[3] numbered as follows:



- Empty 24-hour urine container for tare

Provided by site:

- 24-hour urine sample from study participant
- Scale
- Pipettes and tips or disposable pipettes (10 ml, 5 ml, 1 ml sizes) or plastic transfer pipettes
- Gloves, goggles, and lab coat

Required Equipment:

- University of Michigan OSEH[4] guidelines designate all work done with biological specimens that could produce spray from pipetting be done in a hood, please refer to your site specific OSEH policies.

Responsible Individuals
The NEPTUNE Research Coordinator is responsible for retrieving urine sample from consented participants, returning sample to lab, and processing for storage. In the absence of the Research Coordinator, the Site PI or designated, NEPTUNE trained alternate would provide this service. Local Research Coordinators need to be vigilantly aware of the participant's clinical care needs. Determine in advance if the 24-hour urine is also required for clinical care and coordinate the research sample aliquots appropriately.

Procedure

1. The participant should have been instructed on collecting a 24-hour urine sample. See Appendix K for detailed instructions on 24-hour urine collection.
2. Note start and end time for a maximum timed collection, or "first morning urine" or "random urine collection" for participants unable to provide a full 24-hour sample.

If processing is not able to be completed immediately, please store on ice or refrigerate for a maximum of 4 hours.

3. Weigh the full 24-hour urine collection and note the weight on the study visit worksheet.
4. Weigh the empty 24-hour urine collection container provided for *tare* and enter the tare value on the study visit worksheet.
5. If 24-hour urine sample is larger than one container, the samples must be combined into a single, total urine collection prior to aliquotting. (NOTE: If 2 containers are used, the tare weight must be doubled on the worksheet).

No processing should be done to the 24-hour urine sample – this should be whole, unprocessed/unspun urine.

6. Pour off two 40.0 mL aliquots into the pre-labeled centrifuge tubes:
U1-24 Urine 24hr 50 ml and UQ-24 Urine 24hr 50 ml
7. Gently invert tube **UQ1** 8-10 times to allow dissolution of the protease inhibitor. Remove the cap to allow any air bubbles to escape, replace cap tightly. Place samples aside to complete processing the whole urine sample.
8. Pipette 5 aliquots of 4.5 mLs from the 24-hour urine sample, into the cryovials labeled:
U-24 Urine 24hr Wh
9. Replace the caps, firmly twisting in a clockwise direction.
10. If residual urine does not need to be returned to local labs for clinical care, it may be disposed per OSEH guidelines enforced at participating institution.
11. Note time processed and freeze at -80° C.

Shipping:
Samples should be shipped according to the site-specific scheduled interval for shipments.

All corresponding specimens for each participant ID and visit should be shipped together **on dry ice** following directions in Appendix N for shipping and container provided by NEPTUNE.

Documentation
All corresponding samples for each participant ID should be stored together. If specimen does not adequately fill pre-determined number of aliquots, please document to minimize concerns regarding lost aliquots.

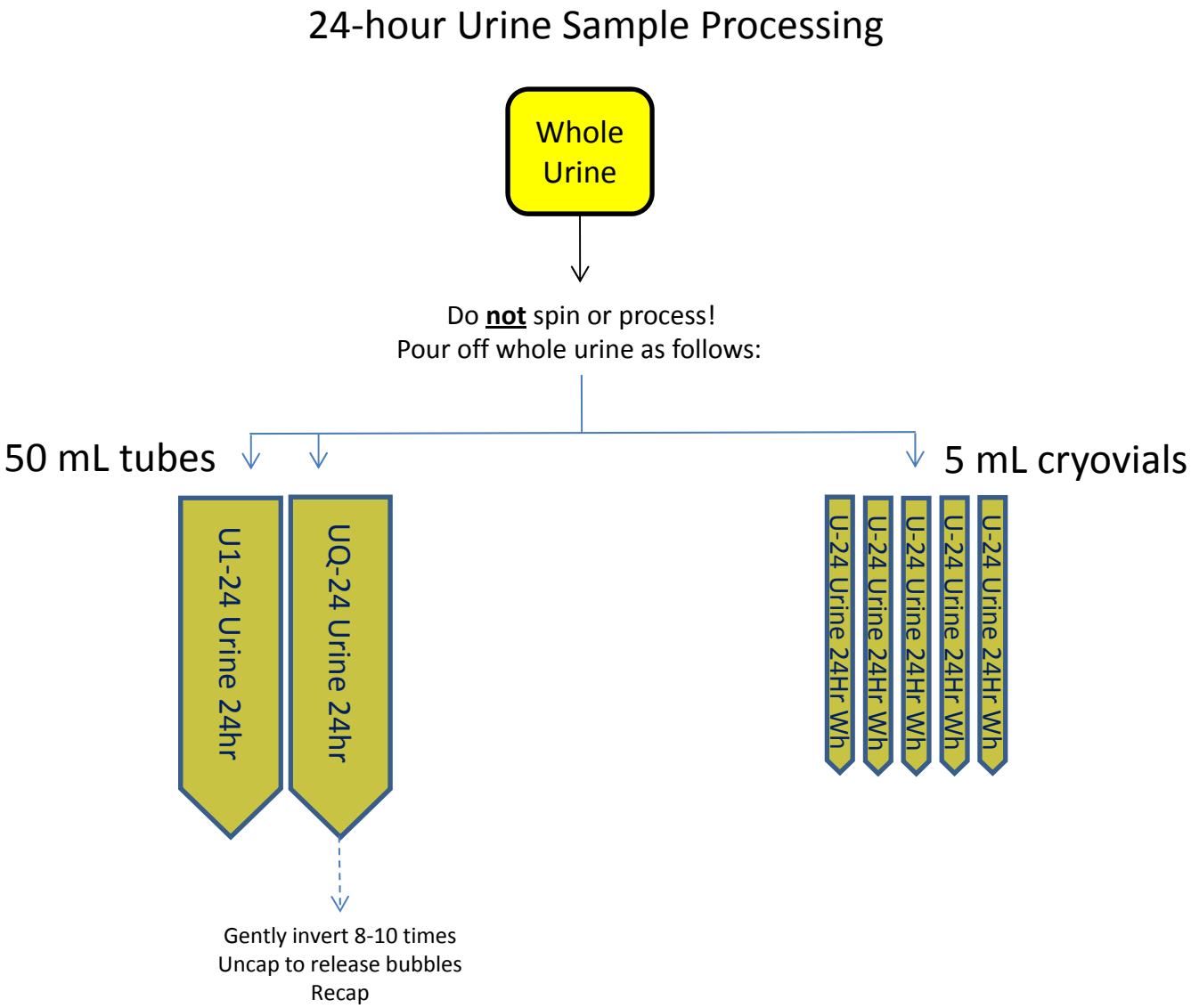
Complete the appropriate Biospecimen CRF corresponding to the study visit, noting any deviations from specimen collection or processing.

26.C.3. References

1. 50.0 mL orange-capped Corning Centrifuge tubes: Corning no. 43290
2. Protease Inhibitor Cocktail: Sigma-Aldrich Catalog: P1860 – 1 mL
3. 5.0 mL Cryovials: Fisher Scientific No. 12-565-167N
4. University of Michigan Occupations Safety and Environmental Health (OSEH) guidelines indicate washing urine and its debris down laboratory sink with adequate water.

Relevant Definitions - None

26.C.4. For Protease Inhibitor Cocktail MSDS See 26.B.4.


24-hour Urine Sample Processing
Whole Urine
Do not spin or process!
Pour off whole urine as follows:
50 mL tubes
5 mL cryovials
U1-24 Urine 24hr
UQ-24 Urine 24hr
U-24 Urine 24Hr Wh
U-24 Urine 24Hr Wh
U-24 Urine 24Hr Wh
U-24 Urine 24Hr Wh
U-24 Urine 24Hr Wh
Gently invert 8-10 times
Uncap to release bubbles
Recap

28. Appendix O. Central Data Entry

28.A. Central Data Entry (CDE) Overview

28.A.1. Objectives

Sites electing to have NEPTUNE study data entered into Velos by the Data Analysis and Coordinating Center (DACC) may do so within a secure system only. The use of the following system is available only to sites which have DACC approval to use CDE after obtaining local IRB approval to transmit de-identified study data.

28.A.2. Secure System Network: MiShare

The method approved by the NEPTUNE DACC to securely transfer study worksheets for CDE will be scanning documents and using the secure collaborative file exchange software MiShare.

MiShare is a secure collaborative file transfer system provided by the Medical Center Information Technology at the University of Michigan Health System. The MiShare infrastructure provides a method approved by the UMHS Compliance Office for UMHS personnel, non-UMHS business partners, and researchers to securely transfer files, including files that contain electronic Protected Health Information ePHI), protected research data, or other sensitive information. Files are encrypted while being uploaded or downloaded, and are encrypted while they are on the MiShare server. (***http://www.med.umich.edu/mishare/help/***)

28.B. MiShare: Preparation of Study Documents

Please abide by the following guidelines in to ensure the proper approved data is shared in an organized manner.

28.B.1. Guidelines for completing data worksheets prior to DACC data transfer:

28.B.1.a. *Legibility*

Please be sure to complete study worksheets legibly using dark ink to ensure readability of scans.

28.B.1.b. *De-Identification*

All forms must be de-identified by excluding the following patient information:

- Name
- Age
- Gender
- Birthdate
- Social Security Number
- Medical Record Number

The DACC will use *only* the Patient Study ID (yy-26609-000-000) or Patient ID to identify patient information in Velos.

28.B.1.c. *Study Worksheets*

- Should be scanned locally
- Should be saved in PDF format

28.B.1.d. *Study Identification*

All forms should be clearly labeled with the following details:

- Study visit number
- Study visit date
- Patient ID (refer to Study ID Numbers, MOP, Part 2)

28.B.1.e. *File Name for Upload*

Files should be named using the Patient ID and the study visit number in the format of PatientID-Visit-Visit# (please include all hyphens)

Example: 000503-Visit-6

28.B.1.f. *Local Documentation*

Maintain local tracking of all forms sent to the DACC using the provided CDE checklist forms (SOURCE)

Instructions for administering worksheets are found in Appendix 16.

28.B.2. Velos Data Entry: Local VS CDE

Although sites approved for central data entry can transfer the majority of the data to the DACC, limited local Velos data entry is necessary. Please refer to the following responsibilities for each study participant (in sequential order):

28.B.2.a. *Local Velos Completion Requirements for ALL sites*

Registration

- Register participants in Velos
- Enroll participant in NEPTUNE with Study ID 10-26609 in Velos
- Assign each participant to the study calendar
- Complete the following Case Report Forms (CRF's):
  - CRF 1: Eligibility Form
  - CRF4A: Race and Ethnicity Fields of the Baseline Participant Information CRF
- Enter and verify Velos date of the ***informed consent EVENT*** is the actual date participant signed the informed consent document

Biopsy

- CRF 11A: Kidney biospecimens CRF (Part I only)

Reconsent

- Participants enrolled under any previous protocol version must be re-consented
- Documentation for re-consent must be noted in Velos (see ConsentV2_UnscheduledEvent in the Velos Training Manual)

Adverse Events

Please see MOP-Part 12 for guidelines for AE reporting. Please note that local sites are required to complete all Velos data entry of NEPTUNE specific AE documentation.

All other worksheets should be scanned and sent to the NEPTUNE DACC for CDE using MiShare

28.B.2.b. ***Central Data Entry Requirements Locally***

Sites must locally complete all guidelines for completing NEPTUNE data worksheets for CDE. Data not complying with these guidelines will be returned for correction prior to CDE.

Please refer to Section 6.B.1.

Local Approval: Sites assume responsibility for:

- Obtaining local institutional review board (IRB) approval to submit documents electronically
- Properly de-identifying all study related documents
- Local reporting of improper PHI transmission

Scanner Accessibility

- Sites must provide a local scanner for scanning study-related worksheets to be submitted for CDE
- Local research teams must be locally trained for scanning, creating, and managing portable document format (PDF) files

28.B.2.c. ***NEPTUNE DACC Central Data Entry***

Forms which can be transferred using MiShare for CDE by the NEPTUNE DACC are:

- Healthcare Provider Information (CRF 3)
- Concomitant Medications Log (CRF 5) for each visit
- Baseline Participant Information (CRF 4A)
- Baseline Family History (CRF 4B)
- Baseline Clinical Information (CRF 4C)
- Baseline Biobank Specimens (CRF 8)
- Baseline Labs (CRF 10)
- PROMIS Survey (CRF 7)
- All Quality Of Life surveys
- Follow-Up participant Info (CRF 13 A)
- Follow-up Family History (CRF 13B)
- Follow-up Clinical Information (CRF 13C)
- Follow-up Biobank Specimens (CRF 14)
- Follow-up Labs (CRF 15)
- V3 Bio specimens CRF
- Withdrawal CRFs

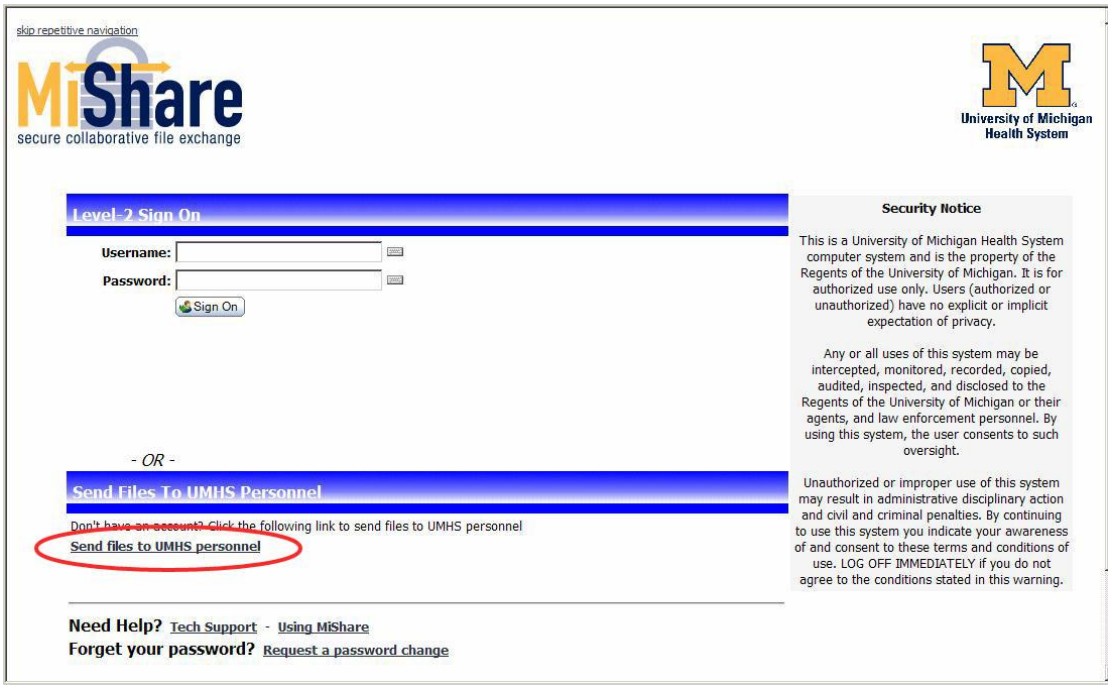
Completed data must be submitted to NEPTUNE DACC within 7 days of study visit completion with the exception of the Baseline and Follow-Up lab Worksheets (CRF's 10 and 15)

28.C. Using Mi-Share to transfer scanned worksheets to the NEPTUNE DACC

28.C.1. Accessing Mi-Share

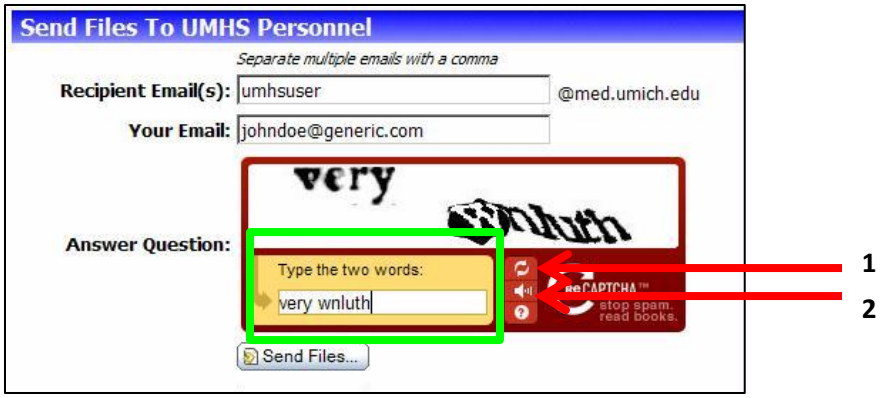
Access MiShare using the following link via any web browser: ***https://mishare.med.umich.edu***

All MiShare users from NEPTUNE sites other than U of M are considered business partners and researchers. Click on the link circled in red in below that says 'Send files to UMHS personnel'. Files are often referred to as *Packages* in MiShare.



28.C.2. Submitting Files

The screen appearing next, *Send Files TO UMHS Personnel – Guest Access* (depicted in the image below), complete the requested fields.



Recipient email address should contain: **klimalex** (address ending not necessary)

Remember to enter the text presented in the Captcha box (outlined in green above). If you have trouble with an image displayed, hit the "Refresh" button (1 above) for a new image or the "Speaker" button (2 above) to hear the text out loud (requires speakers). Once all fields are complete, click Send Files button at the bottom.

28.C.3. Mi-Share Wizard Applet

The first time files are sent using Mi-Share, a screen may appear recommending the installation of the Upload/Download Wizard applet. Using the Wizard has a number of advantages including the ability to drag and drop files, to send large files, and to enable error-checking on the file uploads and downloads. The Wizard only needs to be installed once in the browser. Once the Wizard is installed, it will automatically be used for all future transfers.

It is recommended that sites install the Upload/Download Wizard, a Java Applet because it allows:

- Transfer of files greater than 2GB
- Transfer of multiple files by drag-and-drop
- Performs automatic integrity checking
- Compresses data during transfer

This feature may not be accessible depending upon administrative rights of your workstation.

28.C.3.a. *Wizard Installation*

- Click the *Install the Upload/Download Wizard* link and follow the provided instructions. Internet Explorer users should install the ActiveX applet; other browsers will install the Java applet. Once the Wizard installs, proceed to the next step (6.C.4. Send a Package).

28.C.3.b. *Disabling the Wizard Link*

- To elect to never use the Wizard permanently, click the Disable the Wizard link.
- To avoid using the Wizard for a single session, click the Disable the Wizard for this session only link.

28.C.4. Send a Package

When the Send a Package screen has loaded, provide the Patient ID and Visit Number in the Subject Field and enter any relevant comments to the Note Field to accompany the link for the package to properly identify the contents at the NEPTUNE DACC.

28.C.4.a. *With the Wizard installed*

- Use the Upload/Download Wizard to upload files to the package.

28.C.4.b. *If the Wizard is disabled*

- In the files section, click the Browse (windows) or Choose File (Macintosh) button

- In the new window, locate the file to attach and click the Choose (Mac) or Open (Windows) button
- Click the upload button. The file will upload and appear in the list.
- To add additional files, click the add another file link and then select a file and upload for each additional file as above.

Once all the files are in the package, click the **Send** button.

When the package is sent, the *Send Files to UMHS Personnel – Guest Access* screen will reappear with a message indicating "Sent package with ID '########" OK". This ID number is unique for each package and should be documented locally on the Central Data Entry Checklist Worksheet.

The designated recipient(s) will receive an email message from the MiShare system notifying them a package has been sent.

28.C.5. NEPTUNE Central Data Entry Checklist Worksheets

The CDE Checklist Worksheets have been created for use by sites utilizing the CDE system for NEPTUNE. These worksheets should be completed locally, scanned, and appended as page 1 to the corresponding study participant's visit worksheets. All study visit worksheets should be sent in one PDF file using MiShare.

There are two versions of the Checklist worksheet:

1) Enrollment/Biopsy and/or Baseline Visit
2) Follow-up Visits

One checklist worksheet should be used per participant visit

These worksheets are intended to provide:

- Local checklist of documents to include in the CDE PDF
- Local document tracking details submitted to the DACC
- DACC documentation for incoming data submitted and relevant details

28.D. CDE Checklist: Enrollment/Biopsy [V1/V3] and/or Baseline [V2] Visit

***Please see the reference below for a complete description of each numbered section**

1 Today's Date: _____

Central Data Entry

NEPTUNE Worksheet Completion Checklist:

Enrollment/Biopsy Visits [V1/V3] and/or Baseline Visit [V2]

2 Participant study ID: _____

3 *Please check appropriate visit/s*

☐ Enrollment/Biopsy [V1/V3]	☐ Baseline [V2]

4 Date of Study Visit: _____

Indicate below worksheets completed/not completed for the visit/s selected above

6 Completed? *(Yes or *No)*		7 Doesn't Apply	8 Sent Previously	**5 Enrollment/Biopsy [V1/V3] Worksheets/CRF**
☐	☐	☐	☐	9 V3 Biospecimens CRF
☐	☐	☐	☐	10 CRF 11A Kidney Specimens: Part II ☐ Report Pending
				11 Baseline [V2] Worksheets/CRFs
☐	☐	☐	☐	CRF 4A BL Participant Info
☐	☐	☐	☐	CRF 4B BL Family History
☐	☐	☐	☐	CRF 4C BL Clinical Info
☐	☐	☐	☐	CRF 7 PROMIS Survey
☐	☐	☐	☐	QoL SF36 (adults only)
☐	☐	☐	☐	QoL Peds
☐	☐	☐	☐	QoL Parent of Peds
☐	☐	☐	☐	12 CRF 10 Baseline Labs ☐ *Pending (±30 days)*
☐	☐	☐	☐	CRF 8 BL Biobank Specimens

13 **No: If checked 'No' for any worksheets above, please provide an explanation below for each:*

_____

_____

_____

_____

14 Please send all worksheets for CDE from a particular participant's visit, in one PDF file if possible, using MiShare. This form indicates what worksheets the DACC expects to receive

15 Reference list of NEPTUNE worksheets/data all sites must complete locally in Velos:

- CRF 1 Eligibility Assessment
- CRF 2A Velos Reg. Details
- *CRF 9 Adverse Event
- Informed Consent v2 (add as *'Unscheduled Event'*)
- CRF 11A Kidney Specimens: Part I
- Demographics
- Race/Ethnicity from CRF 4A

16 *Reminder: All AE's must go through DACC prior to submission

17 Unique Package ID:_____

28.D.1. CDE Checklist: Enrollment/Biopsy [V1/V3] and/or Baseline [V2] Visit Worksheet Reference

Header

1 Please enter the date you are transferring worksheets to the NEPTUNE DACC**.**

Corresponding Worksheet Information

2 Please enter the participant ID for which worksheets are being sent.

3 Please select which visit/s worksheets are being sent.

4 Please enter the date of the visit/s indicated in worksheet part 3.

5 The top section of the chart is used if the [V1/V3] visit is indicated in worksheet section 3.

6 Indicate in the corresponding row with a checkmark to record whether the form in each row has been completed or not completed.

7 Indicate in this column for each worksheet that *Doesn't Apply* to the visit/participant in which worksheets are sent.

8 Use this column when submitting worksheets for a previously submitted participant's visit in which some worksheets were previously transferred to the DACC for CDE. (For example, sending the Baseline Lab worksheet CRF 10, which can be collected up to 30 days after the visit took place).

9 V3 Biospecimens Worksheet is used to document the specimen collection done prior to the biopsy procedure

10 A *de-identified* copy of the pathology report should be sent as soon as the complete report is generated and accessible locally. Check box for *report pending* if sending form in section **9** before report is available.

11 This section of the chart is used if the [V2] visit is indicated in section **3**.

12 Baseline Labs can be collected up to 30 days after the study visit, please check the *pending* box if the labs worksheet/CRF10 is not included in the file. Make note to collect if available within the 30 day window.

13 If one of the worksheets for CDE was not completed and is not being sent, please provide an explanation so the DACC can properly document in Velos.

14 Reminder: Send all documents from a participants' visit in one PDF file, including this checklist.

15 This section reminds coordinators which worksheets/data are to be entered locally and not transferred to the DACC for Central Data Entry.

16 Reminder that all AE's must first be brought to the attention of the DACC before submission.

17 *For local site use only:* keep a copy of this checklist for every file you send to the DACC via MiShare. Use this space to record the Unique ID generated after sending the 'package' (file) in MiShare.

28.E. CDE Checklist: Follow-Up Visit [V4-V13]

***Please see the reference below for a complete description of each numbered section**

1 Today's Date: _____

Central Data Entry

NEPTUNE Worksheet Completion Checklist:
Enrollment/Biopsy Visits [V1/V3] and/or Baseline Visit [V2]

2 **Participant study ID:** _____

3 *Please check appropriate visit/s*

☐ Enrollment/Biopsy [V1/V3]	☐ Baseline [V2]

4 **Date of Study Visit:** _____

Indicate below worksheets completed/not completed for the visit/s selected above

6 Completed? (Yes)	6 Completed? (*No)	7 Doesn't Apply	8 Sent Previously	5 **Enrollment/Biopsy [V1/V3] Worksheets/CRF**
☐	☐	☐	☐	9 V3 Biospecimens CRF
☐	☐	☐	☐	10 CRF 11A Kidney Specimens: Part II ☐ Report Pending
				11 Baseline [V2] Worksheets/CRFs
☐	☐	☐	☐	CRF 3 Healthcare Provider Info
☐	☐	☐	☐	CRF 5 Concomitant Meds Log
☐	☐	☐	☐	CRF 4A BL Participant Info
☐	☐	☐	☐	CRF 4B BL Family History
☐	☐	☐	☐	CRF 4C BL Clinical Info
☐	☐	☐	☐	CRF 7 PROMIS Survey
☐	☐	☐	☐	QoL SF36 (adults only)
☐	☐	☐	☐	QoL Peds
☐	☐	☐	☐	QoL Parent of Peds
☐	☐	☐	☐	12 CRF 10 Baseline Labs ☐ *Pending (±30 days)*
☐	☐	☐	☐	CRF 8 BL Biobank Specimens

13 **No: If checked 'No' for any worksheets above, please provide an explanation below for each:*

14 **Please send all worksheets for CDE from a particular participant's visit, in one PDF file if possible, using MiShare. This form indicates what worksheets the DACC expects to receive**

15 Reference list of NEPTUNE worksheets/data all sites must complete locally in Velos:

- CRF 1 Eligibility Assessment
- CRF 2A Velos Reg. Details
- *CRF 9 Adverse Event
- Informed Consent v2 (add as *'Unscheduled Event'*)
- CRF 11A Kidney Specimens: Part I
- Demographics
- Race/Ethnicity from CRF 4A

16 *Reminder: All AE's must go through DACC prior to submission

17 Unique Package ID: _____

28.E.1. CDE Checklist: Follow-Up Visit [V4-V13] Worksheet Reference

Header

1 Please enter the date you are transferring worksheets to the NEPTUNE DACC**.**

Corresponding Worksheet Information

2 Please enter the participant ID for which worksheets are being sent.

3 Please select which study visit worksheets are being sent.

4 Please enter the date of the visit indicated in part 3.

5 The CRFs listed on this chart are for worksheets expected to be completed for Follow-Up study visits and transferred for CDE.

6 Indicate in the corresponding row with a checkmark to record whether the form in each row has been completed or not completed.

7 Indicate in this column for each worksheet that *Doesn't Apply* to the visit/participant in which worksheets are sent.

8 Use this column when submitting worksheets for a previously submitted participant's visit in which some worksheets were previously transferred to the DACC for CDE. (For example, when sending the Follow-Up Lab worksheet (CRF 15), which can be collected up to 30 days post visit date).

9 Use this column to record the prev. data collected is still accurate (no changes) for CRFs 3 and 5

10 CRF 15 Follow-Up Labs can be sent up to 30 days after the visit date; please check the pending box if this worksheet isn't included in the file and the 30 day period hasn't expired.

11 If one of the worksheets for CDE was not completed and is not being sent, please provide an explanation so the DACC can properly document in Velos.

12 Reminder: Send all documents from a participants' visit in one PDF file, including this checklist. Chart above indicates all study worksheets expected for CDE for follow-up study visits.

13 This section reminds coordinators which worksheets/data are to be entered locally and not transferred to the DACC for CDE.

14 Reminder that all AE's must first be brought to the attention of the DACC before submission.

15 *For local site use only:* keep a copy of this checklist for every file you send to the DACC via MiShare. Use this space to record the Unique ID generated after sending the 'package' (file) in MiShare.