I. General Policy and Process Overview
The Nephrotic Syndrome Study Network welcomes proposals from investigators interested in conducting ancillary studies. However, to protect the integrity of the overall study, prioritize the utilization of its resources for scientific advancement, ensure regulatory compliance and monitor participant burden, ancillary studies (AS) must be reviewed and approved by the NEPTUNE Ancillary Study Review Committee (ARC) and the Steering Committee (SC) before inception of research activities or submission of proposal for external funding.

Four steps should be followed in obtaining approval to conduct ancillary studies that involve NEPTUNE: Applicants should 1) explore the potential of their proposal concept or hypothesis and the feasibility of addressing this hypothesis with representatives of the ARC and of the DACC by examining the NEPTUNE data set or infrastructure; (2) work with the NEPTUNE project manager and the Data Analysis Coordinating Center (DACC) to assure availability of data or samples and to establish a budget for the proposed study; 3) submit application for review and approval by the ARC and respond to concerns following review as necessary. Following ARC approval, the AS application is presented to SC for final approval.

See Section V instructions related to the submission process. Section VI details the procedural steps involved in the review.

II. Definition of Ancillary Study
An ancillary study is one based on information or specimens from NEPTUNE participants and/or based on use of the NEPTUNE infrastructure in an investigation or analysis which is relevant to, yet not described in, the NEPTUNE Study protocol. The NEPTUNE infrastructure includes the following: a) scientific and analytical expertise, b) an administrative unit, c) operational structure for NEPTUNE recruitment and retention, d) operational structure organized for collection of NEPTUNE data and biomaterials, and e) a web-based platform.

A typical ancillary study will propose collection of additional data/biomaterials; generation of additional data from existing biomaterials; research analyses not included in the main
NEPTUNE study; or an interventional study utilizing the NEPTUNE cohort as a basis for recruitment. These studies may be submitted by the investigators within or outside of the NEPTUNE investigator consortium.

All ancillary studies must have sufficient non-NEPTUNE funding to support the goals of the ancillary study including costs for study personnel, labs, administration, shipping, data extraction, preparation of data files, statistical analyses, and integration of new data/biomaterials/analyses into the NEPTUNE infrastructure. Administrative costs born by the DACC to support the ancillary study application will be charged to the ancillary study investigator upon start of research activities and/or receipt of Letter of Award (for external funding), whichever comes first. Costs incurred during execution of the research (e.g., sample extraction and shipment, analysis, etc.) will be charged to the ancillary study investigator when incurred. Potential sources of funding include but are not limited to: investigator-initiated research awards from the NIH (e.g. RO1), academic institutions, private foundations and pharmaceutical companies (see Appendix J. Guide for Private Partner Interactions for additional details). Since all ancillary proposals will be directly relevant to the main NEPTUNE study, it is strongly recommended that NEPTUNE investigators with relevant expertise are invited to participate in the development and conduct of research activities in ancillary proposals.

III. Ancillary Study Review Committee (ARC)
The role of the Ancillary study Review Committee (ARC) is to provide feedback to a potential Ancillary Investigator regarding the suitability of the ancillary protocol for integration into NEPTUNE and its likelihood of approval by the SC. The ARC will be comprised of the following members:

- Co-Chairs: Lawrence Holzman and (open position)
- Statistician: Peter Song
- NIH representative (2)
- NEPTUNE Clinical Site Representatives (8): These members will be selected from the participating clinical sites. If a current clinical site representative is from the site submitting the ancillary proposal, he/she will be recused from the review of that proposal.
- Outside Reviewer (1-2): The Chairs may request the input from 1-2 outside peer reviewers, with expertise in the proposed topic, for each ancillary proposal that will not be subjected to a peer scientific review, e.g. proposal with intramural funding.

IV. Steering Committee (SC)
The NEPTUNE SC is comprised of the NEPTUNE Clinical Site PI from each site; a study coordinator; foundation representatives from NephCure Kidney International; NIH project officer(s) from NIDDK / Office of Rare Disease (ORD); and PIs of the Histopathology Reading Center and the Histopathology Digital Archiving Center Pathology Reading. Approval from the SC will be required before an ancillary study can be initiated or submitted to an external sponsor for funding consideration. For the purposes of this process, approval will be defined as a majority (of the combined representation of the Clinical Site PIs and the NIDDK/ORD project officers (Project Scientist and Program Officer)). Each participating site institution will have one vote. Even with SC approval, the participation of each individual site in an ancillary study is optional. However, if a study is based on participation of all sites, then approval of the study must be unanimous.
V. Procedures for Review of Ancillary Study Proposals

A. Proposal Process

1. The overall proposal approval process is outlined in Appendix A and a process checklist is provided in Appendix B.

2. Investigators are strongly encouraged to discuss his/her study idea with the NEPTUNE PI (Matthias Kretzler, kretzler@med.umich.edu), ARC Co-chairs (Larry Holzman, lholzman@mail.med.upenn.edu and open), or ARC member. If necessary, a conference call can be arranged for a larger group discussion prior to proposal submission. Input and advice from these NEPTUNE investigators will provide important guidance in the development of a successful proposal.

3. Fact finding and consultation should be initiated at least four months ahead of the external sponsor’s deadline. Applicants should be aware that complex studies particularly those involving human subjects or the involvement of NEPTUNE clinical sites might take significantly longer to process.

4. Following initial discussion, applicants should submit:
   a. An Ancillary Study Concept Form detailing hypothesis, a short statement of specific aims and experimental approach (Appendix C).
   b. A list of requested data or biosamples. The Ancillary Project Manager will work with the Ancillary Investigator to coordinate initial discussions on availability of samples and/or data, evaluation of study feasibility, burden to the patient, and estimated cost. As appropriate, NEPTUNE tranSMART and/or the Central BioRepository will be consulted.
   c. A budget estimator worksheet will be completed.

5. This proposal will be reviewed by the DACC for:
   a. Needs from NEPTUNE for preliminary data generation for external funding proposal preparation
   b. Data, sample, and budget appropriateness
   c. Suggestions on sites to include (if applicable)
   d. Need for joint CureGN application (if applicable)
   e. MTA/DUA requirement
   f. tranSMART access

6. For studies requiring participation of all clinical sites, investigators must seriously consider feasibility and the interest of NEPTUNE clinical site PIs. Proposals for such studies must include an additional abstract (similar to an NIH abstract) that includes a brief Background, Hypothesis, Specific Aims or Objectives, Methods, and Relavance. This additional abstract will be distributed to all NEPTUNE sites for consideration.

7. Ancillary Project Manager and/or ARC Co-Chairs (Larry Holzman and open) will notify the ancillary investigator whether or not to proceed with formal study Application, as well as indicate if any contingencies were attached to the proposal.
B. Ancillary Application
   1. Once DACC assessment is completed investigators must submit an ancillary study application to the ARC for formal consideration and review within six months. Applicants should use the template and instructions in Appendices E and F, and use the checklist (Appendix B) to assure that AS applications are complete; this checklist should be included with the application. Incomplete proposals will be returned to the investigator.

   2. The investigator should plan to submit a proposal to the ARC well ahead of the external sponsor’s deadline (at least two months).

   3. ARC may require revision of the proposed application; in this situation, revised AS applications should be submitted with a brief cover letter explaining the revision.

   4. All proposals should be emailed to ARC neptunearc@umich.edu and NEPTUNE Principal Investigator, Matthias Kretzler. See detailed instructions for proposal format below.

C. Review and Feedback
   1. The final ancillary application will be reviewed within two weeks of receipt by the DACC for completeness.

   2. Following review by the DACC, the application will be reviewed by the ARC within four weeks. Two members of the ARC and/or external experts will be selected as reviewers and write a brief review of the proposal to be distributed to all ARC members (see Instructions to Reviewers and Review template, Appendix G). Reviewers will present their critique to the full ARC at a monthly meeting. The ARC will discuss, make recommendations for revision, and/or vote to approve.

   3. If recommendations are made for revision, ARC Co-chairs will summarize critiques and make recommendations based on reviews to the investigator, who will then have an opportunity to revise the proposal.

   4. Once approved by the ARC, recommendations of the ARC will be submitted to the SC for final discussion and formal approval. SC members will be provided with the ARC summary and recommendations. If a majority of the SC approves the ancillary study, a letter documenting the ancillary study approval will be sent to the ancillary study investigator for inclusion with application for external funding support. Dissenting members of the SC are encouraged to submit concerns in writing to the ancillary study investigator, especially if the ancillary study receives majority approval. This will give the investigator an opportunity to revise/improve their submission to an external sponsor.

D. Full Proposal Development and Submission
   If approved by the SC, the investigator may submit a full proposal to external sponsors for consideration of funding. In developing the proposal, the investigator should work closely NEPTUNE DACC to ensure that the study is fully integrated into the main study/project.
VI. Criteria Used to Review Ancillary Studies

A. Scientific merit:
   If the proposed AS project will be funded by the applicant without extramural peer review, the ARC will be responsible for evaluating scientific merit and impact of the proposed work. The proposed study must meet requirements of the highest scientific merit and the strength and feasibility of the approach. If the applicant will seek external peer review, the AS proposal will be reviewed only for feasibility of approach and burden to NEPTUNE.

B. Study burden:
   1. The proposed study must be acceptable to the participants (e.g. time, discomfort, privacy);
   2. The proposed study must not adversely affect participant cooperation or compliance with NEPTUNE.
   3. The proposed study must not interfere with other parts of the main NEPTUNE Study;
   4. The proposed study must put minimal demand on scarce NEPTUNE resources such as blood samples (a clear effort to minimize this burden should be documented);
   5. The proposed study must not create a serious diversion of NEPTUNE study resources (personnel, equipment or study samples) or investigator/staff time, either locally or centrally;
   6. The proposed study must require the unique characteristics of the NEPTUNE cohort to accomplish its goals;
   7. The proposing investigators must have adequate resources to effectively complete the project, including but not limited to:
      a) Sufficient budget
      b) Feasibility of utilizing existing NEPTUNE study personnel versus hiring additional personnel will be rigorously reviewed
      c) Staff having the requisite expertise to meet the objectives of the project.
   8. The ancillary study investigators must detail all distributions of specimens, including generation of further data from existing samples, and agree to all elements in the NEPTUNE Ancillary Study Data Use and Material Transfer Agreement (Appendix K), including but not limited to providing a copy of the complete ancillary data set back to the NEPTUNE Study (see Section XII for further details);
   9. The proposed study must not jeopardize the public image of the NEPTUNE Study;
   10. The proposed study must include documented involvement of the NEPTUNE investigators as part of the research team.

VII. NEPTUNE Site Responses to Ancillary Submissions

If the proposed study involves participation from affiliated NEPTUNE clinical sites, the AS application should contain a summary in which the interest of each site in participating in the ancillary study is formally registered. In addition to voting either ‘No’, ‘Yes’, or a ‘qualified Yes’ (with attached comments) each site will indicate one of three levels of desired involvement:
• ‘No interest’
• ‘Partial interest (scientifically engaged, wish to contribute intellectual content, but do not wish to perform additional data collection at our site; no budgetary needs)’
• ‘Full interest (scientifically engaged, wish to contribute intellectual content and to collect data at our site; include in budgetary considerations as appropriate below)
  a) data collection and investigator salary support
  b) investigator salary support alone’

VIII. Ancillary Studies Included in a Training/Career Development Proposal
Ancillary projects proposed as a part of the NEPTUNE Training and Career Development Program will be reviewed by the ARC after the NEPTUNE Scientific Advisory Board has reviewed and prioritized the full proposal. Those proposals prioritized and approved for funding by the full Steering Committee will be reviewed by the DACC and ARC for adjudicated for experimental burden prior to disbursal of funds.

IX. Changes to a Proposed Study
Once an ancillary study is approved, if a change occurs in the structure or concept of the study, including any change in data elements to be collected or analyzed, or any change to study aims, such changes must be disclosed to the ARC and SC, for review and approval before the proposal is submitted to a funding agency or initiation of changes in protocol. Only one such application amendment is allowed: further changes must be done via retraction of approved application and submission of a new application.

X. Human Subjects/Data Confidentiality
Confidentiality of NEPTUNE participants must be guaranteed. Individually identifiable data may not be released. A signed consent must be obtained from every participant in the ancillary study, if the data collection/request is not covered in the original informed consent process for the NEPTUNE study.

A. Any investigator or personnel having access to NEPTUNE subject data should have received an orientation on the NEPTUNE Study confidentiality policy. Key personnel of the ancillary study must be certified in the NIH OHSR or equivalent training course.

B. Per the NEPTUNE Ancillary Study Data Use and Material Transfer Agreement, no attempt shall be made to link subject data to a NEPTUNE participant.

C. A copy of the IRB approval letter for the ancillary study is to be sent to the Ancillary Project Manager at the University of Michigan. If a separate consent form is required for the ancillary study, a copy of the signed ancillary study consent form for each study participant must be included in the NEPTUNE study record. A data file tracking all signed ancillary consent forms must be maintained by the ancillary study and an electronic copy of that file must be delivered to the NEPTUNE Study.

The principal investigator of an ancillary study is responsible for presenting the study to the RC, SC, and/or NIH/ORD as appropriate, monitoring the study to assure continuing compatibility with NEPTUNE Study and serving as a liaison to the NEPTUNE SC. The NEPTUNE SC and administrative team will monitor the development of the ancillary studies, receipt of funding, initiation dates, and progress. A written progress report on
ancillary studies must be made annually to the ARC, SC and/or NIH/ORD. Failure to comply with this policy will be used to prevent publication of results via action of the publication committee.

XI. Handling of NEPTUNE Data and Specimens

All requests, distribution, and analysis of NEPTUNE specimens must be clearly described in the proposal for consideration during review.

At the time of distribution of NEPTUNE specimens and/or information, DACC will make explicit arrangements with the ancillary study Investigator (in accordance with the NEPTUNE Ancillary Study Data Use and Material Transfer Agreement) for the security of these study materials, and for their final disposition at the conclusion of the ancillary study. The safety and confidentiality of the NEPTUNE data at the collaborating institution is the responsibility of the ancillary study Investigator, as is the appropriate disposition of these materials after the study has been completed. Leftover DNA and laboratory specimens are destroyed or returned, and files of NEPTUNE data are returned or deleted, as established at the outset of the collaboration.

If the submitting ancillary Investigator proposes to have a laboratory assay performed on NEPTUNE serum, plasma, urine or DNA in a lab outside of the NEPTUNE Consortium, it is recommended that the Investigator discuss this in advance with one of the ARC Co-chairs, Larry Holzman or open. For an assay to be done outside the NEPTUNE Consortium the submitting Investigator will need to submit both adequate documentation of Quality Control methods at the proposed assay site, and sufficient details on how sample processing will be handled (amounts, type, shipping, frequency, etc.) in an appendix to the application. In addition, both the submitting Investigator and receiving 3rd party are bound by the NEPTUNE Ancillary Study Data Use and Material Transfer Agreement.

The ARC and SC reserve the right to request preliminary data validating an investigator's laboratory method against an external standard. In addition, they may also request outside review by independent experts in the area to certify the QA data presented.

All costs associated with the collection, transfer, analysis and oversight of data collected by an ancillary study will be borne by the ancillary study. Budgets in support of ancillary studies must be sufficient to address all of these requirements regarding ancillary study data. Proposals that do not have sufficient budgets to assure these data management activities will in general not be approved.

XII. Management of Ancillary Study Data

A. All data collected under the auspices of an ancillary study is expected to adhere to the same high standards of quality applied to data collected in the NEPTUNE study. All data from ancillary studies will be scrutinized for quality and consistency using the same mechanisms as are in place for the NEPTUNE.

B. All data from ancillary studies will be made available to the DACC through frequent data transfers. From there, it will be made available to the larger NEPTUNE consortium and other requesting third parties. The frequency and
timing of these transfers will be established prior to the initiation of any ancillary study and included in the study proposal. At a minimum this would be expected to occur at the time of publication or 24 months after transfer of samples or raw data sets, in order to assure the highest quality of data from ancillary studies and enable the tracking of recruitment follow-up of NEPTUNE participants in ancillary studies. The format of data transfer to the DACC must conform to standards compatible with the NEPTUNE data management platform and the NEPTUNE data management group.

C. Any requested period of exclusivity for the data generated by the ancillary study must be documented in the study proposal. Unless stated otherwise, the data will be available to the larger NEPTUNE consortium (via tranSMART or other ancillary study). Guide for Private Partner Interactions for additional details regarding Intellectual Property.

D. At the conclusion of the data analysis and publication of the main (ancillary) study hypothesis, an archival copy of the newly collected data and/or laboratory results not already held at the DACC will be sent to the DACC. This transfer is the responsibility of the ancillary study investigator(s).

E. Once transferred to the NEPTUNE DACC, all ancillary data will become part of the aggregate NEPTUNE data and available to NEPTUNE participant sites and other requesting third parties. Subsequent access to these data will be governed by the NIH ORD data sharing policies.

XIII. Feedback of Results of Ancillary Studies to Participants

Results of ancillary studies shall be reported to participants and/or their physicians if medically useful and in agreement with IRB approval. Such reporting should follow standard NEPTUNE protocol for notification of participants.

XIV. Publications and Presentations

All publications and presentations resulting from ancillary studies must adhere to the requirements of the NEPTUNE Publications and Presentations Policy.

XV. Funding Timeline

Approved ancillary studies must be funded to initiate the study protocol. A written report of the funding status of an approved proposal will be required annually, starting one year after application approval. If funding has not been acquired one year after approval or if the research has not commenced two years after approval, the ancillary study investigator must request approval renewal (based upon active efforts to acquire funding and/or start research) or withdraw the ancillary study. Approval renewal for unfunded or unstarted proposals is not guaranteed. The approval renewal request is made to the ARC, who will present their recommendation to the SC for a final vote.
Appendix A. Expectations for Process and Timeline

You develop a study concept with the Neptune Team
(At least 4 months prior to your funding source deadline)
• Discuss your study concept with NEPTUNE PI, ARC Chair, or ARC Member
• Complete an Ancillary Study Concept Form and Checklist
• Work with Ancillary Study Project Manager on developing your
  List of Requested Data or Biosamples
• Work with Ancillary Study Project Manager on developing a budget estimate

DACC reviews your study concept & materials
(Within 2 weeks of receipt of complete Concept Form and materials)
• Needs from NEPTUNE for preliminary data generation
• NEPTUNE Data, sample, and budget appropriateness
• Suggestions for NEPTUNE sites to include (if applicable)
• Need for joint CureGN application (if applicable)
• NEPTUNE MTA/DUA requirement

You submit an Ancillary Study Application
(At least 2 months prior to your funding source deadline)
• Once DACC reviews, you further develop the Concept Form into an Application
• Use Application Template
• Complete the Checklist and attach to the application

Ancillary study Review Committee (ARC) reviews your application
(4-6 weeks)
• DACC will administratively review for completeness (Within 2 weeks of receipt)
• Two members of the ARC and/or external experts will review the application
• ARC votes to approve (within 4 weeks of DACC administrative review)

Steering Committee (SC) reviews your application
(Within 4 weeks of ARC approval)
• SC reviews ARC recommendations and votes to approve
Appendix B. Ancillary Study Proposal Checklist

Please check items that you completed (double click on box). Your Concept Paper and Application will not be reviewed without this checklist.

Study Concept Development with Neptune Team

☐ Are you submitting a Concept Form at least 4 months before your funding application deadline?

☐ Did you discuss your study concept with the NEPTUNE PI, an ARC Co-Chair, or ARC Member?

☐ Did you complete an Ancillary Study Concept Form?

☐ Did you include a completed “List of Requested Data or Biosamples?”

☐ Did you include a completed “Budget Estimator Worksheet”?

☐ (If Clinical site involvement): Did you include an abstract (similar to an NIH abstract) that includes a brief Background, Hypothesis, Specific Aims or Objectives, Methods, and Relevance that can be sent to participating clinical sites?

☐ Did you include biosketches for key personnel?

Ancillary Study Application

☐ Are you submitting your application at least 2 months before your funding source application deadline?

☐ Are you submitting your application within 6 months of the most recent Concept Form review by DACC?

☐ (If Applicable) Did you provide a one-page response to contingencies described by DACC?

☐ Did you complete Ancillary Study Application Form?

☐ Did you include a Finalized “List of Requested Data or Biosamples”?

☐ Did you include a Finalized “Budget Estimator Worksheet”?

☐ Did you include biosketches for key personnel?
Ancillary Study Concept Form

TITLE PAGE

Study Title:

PIs *(with contact information)*:

Co-Investigators:

Proposed Project Start and End Date:

Abstract *(limited to one paragraph)*:

PART 1. FEASIBILITY

1. Requested Data:

2. Requested Biological Materials *(please complete the data request form)*:

3. Requested Services:
   - Patient Involvement:
   - DACC Involvement: □ Biosample Support □ Biostatistical Support □ Epidemiological Support

4. Funding Source and Application Date:
   - □ Internal funds from your own institution
   - □ Neptune Pilot funding
   - □ NephCure Kidney International-NEPTUNE Ancillary Studies Grant Program
   - □ Private sector funding (specify source):
   - □ Extramural/Intramural Funding
     - If already funded, specify agency and grant number:
     - If planned submission, specify agency and application date:

PART 2. STUDY DESIGN *(2 pages maximum)*:

1. Background and Rationale:

2. Hypotheses and Specific Aims:

3. Design and Methods:
Appendix D. Instructions for Completing the NEPTUNE Ancillary Study Concept Form

The Ancillary Study Concept Form is a 1-2 page document that describes your study concept and initial thoughts on methodology.

**TITLE PAGE**

**Study Title:** Provide a brief title of your proposed study.

**PI(s) (with contact information):** For each principal investigator, provide first and last name, affiliation, email, phone number, and mailing address.

**Co-Investigators:** For each co-investigator, provide first and last name, affiliation, email, phone number, and mailing address.

**Proposed Project Start Date and End Date:** Provide the proposed start and end dates for your ancillary project.

**Abstract:** In a single paragraph, provide a succinct description of your proposed ancillary study.

**PART 1. FEASIBILITY**

1. **Requested Data**

   List the data elements required for this proposal, including specific clinical, pathological, and demographic variables and relevant time points. You may attach a checklist of the available Neptune data, which can be found at [http://www.rarediseasesnetwork.org/NEPTUNE/professional/ancillary/](http://www.rarediseasesnetwork.org/NEPTUNE/professional/ancillary/).

   - If new data collection is requested, describe the procedure for data acquisition. If applicable, specify which site(s) would be involved and number of subjects per site.

2. **Requested Biological Materials**

   List the biological materials required for this proposal, including: a) specimen type, b) minimal amount required, c) sampling time point(s), and d) requirement for frozen vs. previously thawed samples. You may attach a checklist of the available bio-specimens, available at [http://www.rarediseasesnetwork.org/NEPTUNE/professional/ancillary/](http://www.rarediseasesnetwork.org/NEPTUNE/professional/ancillary/).

   - If new collection of biological material is requested, describe the procedure for sample acquisition. If applicable, specify which site(s) would be involved and number of subjects per site.

3. **Requested Services:** This section relates to the utilization of the NEPTUNE resources, overall cost estimates, and impact on the Core Study.

   **Patient Involvement:** Provide a rationale for additional procedures or visits, estimated time of patient participation, and the effort and estimated time required of site recruitment coordinators. If the study involves a new questionnaire, provide a copy of the proposed questionnaire with this application.
DACC Involvement: Please check all appropriate boxes and describe the effort and estimated time required of the Data Analysis and Coordinating Center (DACC). This includes project management, subject identification, dataset preparation and/or statistical analysis.

4. Funding Source and Dates: Check the appropriate funding source. If you have extramural/intramural funding, provide relevant grant numbers. If you plan to submit a grant application, provide grant due date and funding source/mechanism.

PART 2. STUDY DESIGN

1. Background and Rationale: Briefly describe why your study is worth pursuing.

2. Hypotheses and Specific Aims: Clearly state your study hypotheses and specific aims.

3. Design and Methods:
   - Describe the plan for data acquisition.
   - Describe sample collection and handling.
   - Describe specific assays and experiments proposed.
   - Describe planned quality control measures.
TITLE PAGE

Study Title:

PIs (include contact information):

Co-Investigators:

Proposed Project Start and End Date:

Abstract (limit to one paragraph):

PART 1. FEASIBILITY (1 page maximum)

1. Requested Data:

2. Requested Biological Materials (please include the completed data request form):

3. Requested Services:
   Patient Involvement:
   DACC Involvement: □ Biological Sample Support □ Biostatistical Support □ Epidemiological Support
   Cost Estimate:

4. Funding Source and Application Date:
   □ Internal funds from your own institution
   □ Neptune Pilot funding
   □ NephCure Kidney International-NEPTUNE Ancillary Studies Grant Program
   □ Private sector funding (specify source):
   □ Extramural/Intramural Funding
     If already funded, specify agency and grant number:
     If planned submission, specify agency and application date:

5. IRB Approval:

PART 2. STUDY DESIGN (3 pages maximum excluding references):

1. Background and Rationale:

2. Hypotheses and Specific Aims:

3. Design and Methods:

4. Statistical Analysis, including power analysis and sample size justification:

5. Anticipated Results and Project Timeline:

6. Data Sharing Plan:

7. References (limited to 15 maximum)
Appendix F. Instructions for Completing the NEPTUNE Ancillary Study Application

The Ancillary Study Application is limited to 5 pages, excluding references, biosketches, and, if applicable, your one-page response to contingencies described by DACC. Incomplete applications will not be reviewed. Requirements for each item on the application are provided below.

**TITLE PAGE**

**Study Title:** Provide a brief title of your proposed study.

**PI(s) (with contact information):** For each principal investigator, provide first and last name, affiliation, email, phone number, and mailing address.

**Co-Investigators:** For each co-investigator, provide first and last name, affiliation, email, phone number, and mailing address.

**Proposed Project Start Date and End Date:** Provide the proposed start and end dates for your ancillary project.

**Abstract:** *In a single paragraph,* provide a succinct description of your proposed ancillary study. Note that if your study is approved by the ancillary study committee, the abstract will become public and may appear on the NEPTUNE study website.

**PART 1. FEASIBILITY (1 page maximum)**

1. **Requested Data**

   List the data elements required for this proposal, including specific clinical, pathological, and demographic variables and relevant time points. You may attach a checklist of the available Neptune data, which can be found at [http://www.rarediseasesnetwork.org/NEPTUNE/professional/ancillary/](http://www.rarediseasesnetwork.org/NEPTUNE/professional/ancillary/).

   - If new data collection is requested, describe the procedure for data acquisition. If applicable, specify which site(s) would be involved and number of subjects per site.

2. **Requested Biological Materials**

   List the biological materials required for this proposal, including: a) specimen type, b) minimal amount required, c) sampling time point(s), and d) requirement for frozen vs. previously thawed samples. You may attach a checklist of the available bio-specimens, available at [http://www.rarediseasesnetwork.org/NEPTUNE/professional/ancillary/](http://www.rarediseasesnetwork.org/NEPTUNE/professional/ancillary/).

   - If new collection of biological material is requested, describe the procedure for sample acquisition. If applicable, specify which site(s) would be involved and number of subjects per site.

3. **Requested Services:** This section relates to the utilization of the NEPTUNE resources, overall cost estimates, and impact on the Core Study.
**Patient Involvement:** Provide a rationale for additional procedures or visits, estimated time of patient participation, and the effort and estimated time required of site recruitment coordinators. If the study involves a new questionnaire, provide a copy of the proposed questionnaire with this application.

**DACC Involvement:** Please check all appropriate boxes and describe the effort and estimated time required of the Data Analysis and Coordinating Center (DACC). This includes project management, subject identification, dataset preparation and/or statistical analysis.

**Cost Estimate:** Provide the estimate of the total yearly cost for your study based on the Neptune Cost Estimate Worksheet. Note that once your study is approved, the DACC will help you develop the final budget.

4. **Funding Source and Dates:** Check the appropriate funding source. If you have extramural, or intramural funding, provide relevant grant numbers. If you planning to submit a proposal for funding, provide grant due date and funding source/mechanism.

5. **IRB Approval:** If IRB-approved, provide IRB name and approval date. If you do not have IRB approval, please describe your plan for obtaining IRB approval for this study. Please note that although IRB review is not required at the time of this application, the letter of approval must be provided before data and specimens can be released.

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**PART 2. STUDY DESIGN (3 pages maximum excluding references)**

1. **Background and Rationale:** Briefly describe why your study is worth pursuing.

2. **Hypotheses and Specific Aims:** Clearly state your study hypotheses and specific aims.

3. **Design and Methods:**
   - Describe the plan for data acquisition.
   - Describe sample collection and handling.
   - Describe specific assays and experiments proposed.
   - Describe planned quality control measures.

4. **Statistical Analysis, including power analysis and sample size justification:** Describe your data analysis plan and justify why you feel your proposed study is adequately powered to address the research hypotheses.

5. **Anticipated Results and Project Timeline:** Describe your anticipated results and provide a clear timeline for the project. Include a projected publication date.

6. **Data Sharing Plan:**
   - The plan for sharing newly acquired data, including new clinical, biochemical, genetic, and/or other data types will comply with NEPTUNE policy of data transfer 12 months after data generation or at time of accepted publication.
   - The use of tranSMART will be offered as an incentive to share data early for integration and interrogation of data. An option of a 12 month protected window for the data (visible only to the ancillary investigator) will be allowed, prior to wider distribution and access.

7. **References (15 maximum):** Provide a maximum of 15 key literature references in support of your proposal.
Appendix G. Ancillary Study Review Instructions and Form

Dear Reviewer,

Thank you for your willingness to assist in the Neptune Ancillary Study review process. This page has been created to assist you with the evaluation sheet. Please refer to the full Neptune Ancillary Studies Policy for additional details.

In your review, please answer the following primary questions:

1. **Will the proposal strengthen the Neptune mission and specific aims?**

2. **Will the proposal appropriately use resources of Neptune?** Consider the following:
   - Is the proposed study feasible and does it use the Neptune resources wisely?
   - Will the ancillary study be strengthened by the use of the Neptune subjects and infrastructure?
   - Are proper precautions made to maximally preserve limited samples and assure high quality of generated data?

3. **Will the proposal negatively affect the core Neptune infrastructure?** Assess if the proposed study has a significant potential to negatively impact the main study. For example, a study that requires high intensity visit schedule of the study patients at the time of enrollment may be too large a burden on the patient or the local study team and negatively impact recruitment or retention.

4. **Is the proposal scientifically valid?** Assess the strengths and weaknesses of the proposed specific aims. Are the hypotheses and scientific questions significant and of high impact? Are the methods for data acquisition, sample assays, and experiments scientifically justified? Is the proposed study adequately powered? Is the data-sharing plan adequate?

   Studies that will be submitted for extramural review and funding (e.g. NIH, National Kidney Foundation) do not need a detailed scientific review. Studies that will not be subjected to scientific peer review due to a plan for local or unfunded efforts must have a detailed scientific review incorporated into the ancillary studies review process.

**Overall Recommendation:** Your recommendation options are to request more data, recommend a minor or major protocol modification prior to final decision, approval or rejection. Based upon the primary reviewers’ recommendations, the Ancillary Studies Committee and subsequently the Steering Committee will make the final determination.

**Comments:** Please provide justification for your overall recommendation. If applicable, provide a list of requested revisions.

**Timing:** Please complete your review within 2 weeks and return your evaluation to Tina Mainieri (tmainier@med.umich.edu). All reviewers for a proposal will be invited to join the subsequent Ancillary Study Committee meeting to discuss their recommendations.
Neptune Ancillary Study Evaluation Form

Study Title: 

Applicant: 

Review Date: 

1. Will the proposal strengthen the Neptune mission?

2. Will the proposal appropriately use resources of Neptune?

3. Will the proposal negatively affect the core Neptune infrastructure?

4. Is the proposal scientifically valid?

Overall Recommendation:

☐ Approve

☐ Revise (please specify what would you like to see in a revised application?)

☐ Disapprove (please specify what would you like to see in a revised application?)

Additional Comments:
Appendix H. Neptune Ancillary Studies Review Committee (ARC)

Laura Barisoni (U Miami)
Dan Cattran (UHN-Toronto)
Mike Flessner (NIDDK)
Debbie Gipson (U Michigan)
Marie Hogan (Mayo)
Rick Kaskel (Montefiore)
Richard Lafayette (Stanford)
Kevin Lemley (USC)
Laura Mariani (U Michigan)
Marva Moxey-Mims (NIDDK)
Patrick Nachman (UNC)
John O’Toole (Case Western)
Heather Reich (UHN-Toronto)
Matthew Sampson (U Michigan)
James Shayman (U Michigan)
Peter Song (U Michigan)
Howard Trachtman (NYU)

Chair: Larry Holzman (U Penn)
NEPTUNE welcomes collaborations with Private Partners to advance the understanding and treatment of nephrotic glomerular diseases. As a consortium of academic institutions, however, NEPTUNE itself does not directly establish collaborations with Private Partners as an entity separate from its constituency.

The following policy and procedures guide the interaction of Private Partners with NEPTUNE in order to preserve the scientific validity and data integrity of the consortium.

1. For purposes of these policies, Private Partners are defined as third party entities with a vested interest in the outcome or results of the interaction. For example, a company interested in validating a new proprietary test would qualify as a Private Partner. A central laboratory running an assay would NOT qualify as a Private Partner (only a service provider).

2. Interactions with Private Partners must be done under the Ancillary Study mechanism established within the NEPTUNE consortium and follow all policies and procedures (see NEPTUNE Ancillary Studies Policy and Procedures).

3. Ancillary studies involving Private Partners must be proposed to the NEPTUNE consortium by an academic Principal Investigator (PI).

4. An academic PI-Private Partner collaborative ancillary study must be approved by the NEPTUNE consortium using the NEPTUNE mechanism for approval of ancillary studies, prior to initiation of the study. This applies to studies deemed to be initiated by the academic PI or by the Private Partner.

5. A Private Partner interested in proposing their own ancillary study that will use NEPTUNE infrastructure or resources (i.e., NEPTUNE bio-specimen resources and/or NEPTUNE resources held in silico) must interface with NEPTUNE via an academic investigator already within NEPTUNE. This investigator will be recognized by NEPTUNE as the academic PI proposing the ancillary study, in which the Private Partner is a scientific collaborator.

6. The academic PI of the ancillary study will administer the responsibility for adherence to NEPTUNE Ancillary Studies Policy and Procedures by the Private Partner. This administrative responsibility of the academic PI to NEPTUNE must be formalized before the initiation of the ancillary study by agreement between the academic PI's home institution and the Private Partner to incorporate the following:

   • NEPTUNE cannot be bound by any exclusive rights to the use of NEPTUNE infrastructure and/or resources by a Private Partner.

   • The intent to derive Intellectual Property from the use of NEPTUNE infrastructure and/or resources by a Private Partner cannot restrict in any way the use of NEPTUNE infrastructure and/or resources by others towards their own interests.

   • Intellectual Property can be developed from the use of NEPTUNE infrastructure and/or resources by a Private Partner. However, if requested, an unrestricted research use license of this Intellectual Property must be provided to other academic investigators for
their own use of NEPTUNE infrastructure and/or resources towards their own research interests.

- All data derived from the use of NEPTUNE infrastructure and/or resources by a Private Partner must ultimately be shared with NEPTUNE for use in the public domain. Data is to be deposited with the NEPTUNE DACC. A timeline for data transfer to NEPTUNE and rationale for proposed timeline may include a proprietary period to develop Intellectual Property from the data. The timeline and rationale must be stated in the ancillary study proposal, for review by the NEPTUNE Ancillary Study Committee and final approval by vote of the NEPTUNE Steering Committee. In the absence of such a timeline, the default timelines included in the Ancillary Study Policy and Procedures document will be in effect.

- Publication of the results of the ancillary study in the public domain must be a goal of the ancillary study. Use of NEPTUNE infrastructure and/or resources solely to derive Intellectual Property for a Private Partner in the absence of attempts to publish the results of the ancillary study in the public domain is counter to the charter of NEPTUNE. Manuscript(s) resulting from the ancillary study must be reviewed and approved for submission for external review by the NEPTUNE Publications and Presentations Committee prior to submission for external review.
Appendix K. NEPTUNE ANCILLARY STUDY
DATA USE AND MATERIAL TRANSFER AGREEMENT

The Regents of the University of Michigan, a constitutional corporation of the State of Michigan with a principal address at 3003 S. State Street, Ann Arbor, MI 48109 ("Provider"), acting as the Data Analysis and Coordinating Center ("DACC") for the Nephrotic Syndrome Study Network ("NEPTUNE"), agrees to provide _________________________________ ("Recipient") with certain research material for use by its scientist, _________________________ ("Scientist"), subject to the terms and conditions set forth in this Material Transfer Agreement (the "Agreement").

1. This Agreement applies to the transfer of specimens, any progeny and unmodified derivatives thereof, and/or data that have been de-identified pursuant to the requirements of the Health Insurance Portability and Accountability Act (collectively, the "Material") for use by Scientist to conduct an ancillary study (the "Research") that has been reviewed by the NEPTUNE Ancillary Study Review Committee ("ARC") and approved by the NEPTUNE Steering Committee ("SC").

2. The transfer of the Material constitutes a non-exclusive license to use the Material solely for the Research.

3. Recipient and Scientist agree that the Material shall only be used for purposes of the Research within Scientist’s lab under conditions as articulated in the NEPTUNE Ancillary Studies Policy and Procedures (attached and incorporated herein as Appendix A). Uses of the Material beyond those anticipated in the Research require submission of an amendment for review and approval to the ARC and SC.

4. Recipient agrees that no person authorized to use the Material under this Agreement shall make available any portion of the Material to any person or entity other than laboratory personnel under the Scientist’s immediate and direct control. No person authorized to use the Material shall be allowed to take or send the Material to any location other than the Scientist’s laboratory without the Provider’s prior written consent.

5. Under no circumstances shall Recipient or any person to whom Recipient directly or indirectly discloses the Material make any attempt to link the Material to any individual, whether living or deceased, associated with the Material. In the event Recipient inadvertently identifies an individual whose information is part of the Material, Recipient shall promptly notify Provider of such identification.

6. Recipient will promptly report to Provider any identified use or disclosure of the Material that is inconsistent with the terms and conditions of this Agreement.

7. PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE MATERIAL WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS. Unless prohibited by law, Recipient assumes all liability for claims for damages against them by third parties that may arise from the use or disclosure of the Materials except that, to the extent permitted by law, the Provider shall be liable when the damage is caused by the gross negligence or willful misconduct of the Provider.

8. Recipient shall establish appropriate safeguards to ensure that the Material are used or disclosed only in compliance with the terms and conditions of this Agreement and with all applicable
statutes and regulations, including without limitation current NIH guidelines and any regulations or guidelines pertaining to research with recombinant DNA, that may be applicable to the Material.

9. Recipient agrees, per the NEPTUNE Ancillary Studies Policy and Procedures, to provide Provider with copies of all data generated by Recipient’s Research. Recipient and Scientist understand and agree that such data will be maintained by the DACC and made available to NEPTUNE participant sites and other requesting third parties.

10. This Agreement is not assignable.

11. This Agreement is effective as of the last signature date and shall terminate when all of the Material provided by Provider to Recipient are destroyed or returned to Provider, or, if it is infeasible to return or destroy the Materials, protections, reviewed and approved by Provider, are extended to such Materials.

WHEREFORE, the parties, through their authorized representatives, hereby accept and agree to the terms and conditions of this Agreement.

FOR THE REGENTS OF THE UNIVERSITY OF MICHIGAN

By: ____________________________
Name: __________________________
Title: ___________________________
Date: __________________________

FOR RECIPIENT
[Note: must be signed by an authorized officer.]

By: ____________________________
Name: __________________________
Title: ___________________________
Date: __________________________

Read and Acknowledged
[Enter Name of Recipient’s Scientist]

Scientist: _______________________
Date: ______________________