Childhood Liver Disease Research Network (ChiLDReN)

Ancillary Studies Policy

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1. Background
The ChiLDReN studies include well-characterized populations of individuals with various pediatric liver diseases for whom data are collected and stored by the Scientific and Data Coordinating Center (SDCC) and biological samples are processed and stored in the NIDDK-sponsored biospecimen repository. To make the best possible use of this extraordinary resource, the ChiLDReN Steering Committee (SC) encourages investigators, both internal to the network and external, to develop ancillary studies. The policies governing the use of data and/or biological specimens in ancillary studies are detailed in this document.

2. Definition of an ancillary study
An ancillary study is defined as one that uses ChiLDReN subjects and/or data and/or biological specimens collected from them for a purpose other than intended by ChiLDReN and/or written into its protocols and procedures; or as deemed by the NIDDK and ChiLDReN as the most efficient and expeditious avenue to carry out an ancillary study. In general, ancillary studies are characterized as being outside the specific scientific objectives of the ChiLDReN studies, potentially requiring a separate consent form, placing an additional burden on participants, and/or being funded by a mechanism that is separate from the ChiLDReN funding mechanisms. Most ancillary studies are expected to involve analysis of existing data or new measurement on existing specimens. However, an ancillary study may require new data collection (i.e. additional to that required by the ChiLDReN protocols and CRFs) from subjects, such as a new questionnaire to complete, or a new biologic specimen to be obtained from subjects. An ancillary study may involve all ChiLDReN subjects of a certain type or class or subjects at a subset of ChiLDReN clinical sites.

3. Function of the Ancillary Studies Committee
The Ancillary Studies Committee (ASC) is a subcommittee of the ChiLDReN Network Steering Committee (SC).

The Administrative Core supports the operations of the ASC by receiving submitted applications for ancillary studies, administering the process for review of submitted applications, writing correspondence for the Committee and notifying the SC of voting results.

The Administrative Core will provide the SDCC with all Ancillary Study Proposal approvals/disapprovals and all status updates. The SDCC supports the operations of the ASC by maintaining the lists of ancillary studies and allocated or committed samples and archiving the correspondence files related to the Committee’s activities.

The Ancillary Studies Committee (ASC) is charged with facilitating the use of ChiLDReN resources to achieve the greatest scientific benefit possible. To do this, the committee considers several important factors in each proposal.

a. Scientific merit. Using the Committee’s expertise, a proposal will be judged as having the scientific merit to warrant use of the resources being requested. When developing the proposal, the investigator should clearly state the goals of the study in terms of what the expected results will add to the scientific understanding of childhood liver disease and/or what gaps in knowledge will be closed by the research. The scientific description of the concept proposal is limited in length to two or four pages (depending on type of submission [described in section 4.3]), so great care must be given to conciseness and clarity of writing.
b. Justification of the burden being placed on ChiLDReN. By definition, all ancillary studies will use ChiLDReN infrastructure and/or reposited resources. If those resources are not exhaustible, such as electronically stored data, the burden is minimal, the cost of providing the resource minimal, and justification for their use not very critical. If they are scarce and non-renewable (i.e. frozen liver specimens), the justification for their use is very important and will determine if they are released. If the proposal calls for gathering new data or specimens, the difficulty and costs of undertaking the study (i.e. IRB submissions at each participating center, additional burdens placed on patients and family/guardians in relationship to the existing study demands and study personnel, administering questionnaires, collecting specimens) are substantial, then the need for equally substantial justification is placed on the investigator proposing the study.

c. Feasibility. The diseases being studied in ChiLDReN are rare and thus the numbers of samples available may be limited. If an investigator proposes a study that will require more samples than will be available to achieve a scientifically valid conclusion, the inevitable outcome will be rejection of the study concept at the level of the preliminary review. If completing the study would exhaust any given resource, submission of the proposal will only be allowed if the study has outstanding scientific merit and will result in major scientific advances.

d. Will the study be completed? The Committee will consider whether the resources, funding, expertise, etc. of the investigative team should reasonably permit completion of the proposed work.

e. Plans for funding. Many ancillary studies are approved contingent upon obtaining funding. Samples are promised and encumbered but not delivered until the funding is guaranteed (i.e. NOGA is transmitted). For example, the Committee will write a letter in support of a NIH grant application stating that the samples being requested are available to the investigator if the grant is funded. Investigators who are responding to a program announcement or applying for funding should gain approval for the ancillary study before submitting their application to a funding organization. A funded study will not necessarily be approved for distribution of samples if the request comes after the funding has been granted. If the study is to be supported by other than a federal agency, the investigator must show that sufficient funds are available and obtain an affidavit from the local institution's grant office to that effect. No study will be approved without a budget and proof that the funds are available to meet the budgetary need. **PLEASE NOTE:** If the funding source or service is from a private party (i.e: industry, foundation, etc.), then a formal agreement must be executed between the PI, the PI's institution, and the private party. The agreement will need to be reviewed by the NIDDK with respect to the preservation of the PI's academic independence for data analysis and preservation of full academic freedoms with regard to publication rights and privileges.

f. Conflict or major scientific overlap with another study. Conflict is apparent in several ways. The most obvious is the need to unblind results of a clinical trial before the trial is completed. Another is the need for samples that have already been promised to another study. Major scientific overlap occurs when a study proposes to do nearly what an ongoing study is doing. To gain approval for this would require providing evidence that some advance in technique or technology will lead to better or more valid results. An ancillary study that could interfere with completion of the ChiLDReN objectives will not be approved.
4. Composition, Structure, and Operations of the Ancillary Studies Committee

4.1 Ancillary Studies Committee membership, election, and voting

The ASC is comprised of 9 voting members and the Research Administrator as follows:

- One Chairperson (PI or Co-I from a site)*
- One Vice-Chairperson (PI or Co-I from a site)*
- One SDCC representative
- One NIDDK representative
- Four site PIs or Co-investigators*
- One site pathologist (cannot be from same site as other committee investigators)
- Research Administrator (from Administrative Core; non-voting member)

* limit PIs or Co-Is to one per site

Members will serve for 3-year terms, in most cases. The Chair and Vice Chair will serve staggered 3-year terms, with the Vice Chair assuming the Chair position when the Chair cycles off the committee. The terms of these two positions may be extended with permission from NIDDK and the Executive Committee. The members from the SDCC, NIDDK and Administrative Core may serve for the duration of the ChiLDReN grant cycle.

Committee members including the Chair and Vice-Chair will primarily be chosen by election, though in some cases, the Chair and Vice-Chair positions may be appointed by the Executive Committee. The Admin Core will coordinate the election process. When there is a vacancy on the committee, SC members can volunteer or be nominated and will be listed on an email ballot to be circulated by the SDCC for an email vote by the SC voting members. There will be a maximum of three nominations per position. In the case of tie votes, the Executive Committee will make the final decision.

Beginning with the funding period starting June 1, 2017, elections will typically be held during the months of April to May and the results discussed on the May SC conference call. New committee terms will begin on June 1 of each year. Other modifications to term dates will be made, as needed, and only if approved by the Executive Committee.

4.2 Ancillary Studies Committee Operations

The ASC will meet regularly by email and/or conference call to review and vote on all proposals received in a given review period.

Ancillary proposals will be accepted six times each year. Three submission deadlines will be the same as the NIH R01 deadlines, which will provide a 4-month interval prior to the next NIH submission deadline (e.g., Ancillary Study deadline of February 5 is four months ahead of R01 deadline of June 5). The remaining three deadlines will be evenly distributed between the NIH deadlines. Results of the ASC Review will be returned to each proposal PI approximately two months after the submission date.

ASC submission dates are noted below in section 5.1.

4.3 Types of Reviews Conducted by the ASC

The ASC will conduct reviews in one of two ways, based on information provided by the proposal PI at submission. Each proposal PI will be asked to indicate whether the proposal will be submitted to NIH (or other federal agencies) for...
funding, and therefore, will undergo peer review by that agency; or if the proposal will be
funded by sources other than federal agencies (e.g. department funds, foundations, etc.,) in
which case the AS Committee will perform the peer review.

4.3.1 Proposals that will be submitted to NIH and other federal agencies
For proposals that will be submitted (if approved by ChiLDReN) to NIH or other federal
external funding agencies to provide funding for the proposal, and will undergo rigorous
peer review at the NIH study section (or equivalent), the primary purpose of the
ChiLDReN ASC review will be to 1) ensure availability and appropriate use of
ChiLDReN infrastructure and biospecimen resources, if the proposal receives a
fundable score from the study section; and 2) provide constructive feedback to the
proposal PI that will strengthen his/her application to NIH. These proposals can be up
to two pages in length.

4.3.2 Proposals that will be funded by funding sources other than federal
agencies
For proposals that will be funded by non-federal sources, the ChiLDReN ASC will
conduct a thorough and rigorous scientific review of the proposal, addressing all points
typically covered by a NIH Study Section. These proposals can be up to four pages in
length.

5. Proposing an ancillary study
Any investigator in ChiLDReN, whether a center PI or a Co-investigator named as such by any
center, may submit an ancillary study proposal. Any other investigator (i.e. from outside of a
ChiLDReN center or working within a ChiLDReN center but not a named investigator) wishing
to conduct an ancillary study must submit the proposal with a ChiLDReN center grantee PI’s
endorsement. By giving his/her endorsement, a ChiLDReN PI agrees to be the Liaison
between the investigator and ChiLDReN and to be responsible for ensuring that all ChiLDReN
Network policies are met. If a ChiLDReN PI is an active participant or co-investigator in the
ancillary study, it is appropriate that he/she submit the proposal.

The ChiLDReN Ancillary Study Application Forms, including the ChiLDReN ANCILLARY
STUDY PROPOSAL FORM, the ChiLDReN DATA REQUEST FORM, and the ChiLDReN
SPECIMEN REQUEST FORM, are available on the ChiLDReN public website

5.1. To determine the feasibility of the proposed Ancillary Study, it is required that any
investigator who is contemplating submission of an Ancillary Study (prior to full
submission of the Ancillary Study) to ChiLDReN should complete two steps prior to
submission:
• Step One: The proposal PI or AS Liaison (see section 11.4 below) will review the
SDCC website’s list of ancillary studies for any potential overlap between the proposed
study and other studies within ChiLDReN. The proposal PI or AS Liaison will check
active studies, completed studies, and reviewed rejected studies, and assure the idea
has not been previously discussed by the network and that it is not being addressed in
some other way. Documents > Committees > Ancillary Studies Committee
• Step Two: The proposal PI or AS Liaison will submit a Data and Specimen Request
Form to the SDCC via ChiLDReN-Project-Team@arborresearch.org by the due dates
listed below. This is a required submission that is due approximately six weeks before the planned ChiLDReN submission deadline. The SDCC will work with the investigator to help determine if the needed data and/or specimens are available.

- Data and Specimen Request Forms must be received by the SDCC at the email address above by the following dates (or the following business day if these dates fall on weekend or holiday):
  - Jan 15 (full proposal packet will be due to ASC on Mar 1)
  - Mar 15 (full proposal packet will be due to ASC on May 1)
  - May 15 (full proposal packet will be due to ASC on Jul 1)
  - July 15 (full proposal packet will be due to ASC on Sep 1)
  - Sept 15 (full proposal packet will be due to ASC on Nov 1)
  - Nov 15 (full proposal packet will be due to ASC on Jan 1)

5.2. Completion of the Ancillary Study Application Forms. ONLY IF the request to the SDCC is deemed feasible, the following should be submitted on the AS application forms:

a. The principal investigator (PI) for the ancillary study and his/her institutional affiliation.

b. Names of other key investigators for the ancillary study and their institutional affiliations.

c. Name of the ChiLDReN SC PI grantee or corresponding PI grantee who will be the liaison or co-investigator for the study (if different from study PI).

d. The study title, objectives including primary outcome measures, and estimated start and end dates.

e. The ChiLDReN population to be studied.

f. A Concept Sheet describing the research hypothesis, design and methods for achieving the study objectives (2 or 4-page maximum length (per section 4.3) - this is to be a concise, well organized description similar to the specific aims page of a NIH grant). An additional 2 pages of preliminary data supporting the proposal may be submitted, and is recommended to ensure a well-informed review.

g. Sample size, with justification.

h. The ChiLDReN infrastructure and resources (data and specimens) being requested.

i. The funding source and status of funding for the ancillary study; any unreimbursed work or personnel time expected of ChiLDReN or SDCC must be specified so that the ASC can evaluate whether ChiLDReN should assume that unreimbursed work or personnel time. **PLEASE NOTE:** If the funding source or service is from a private party (i.e.: industry, foundation, etc.), then a formal agreement must be executed between the PI, the PI’s institution, and the private party. The agreement will need to be reviewed by the NIDDK with respect to the preservation of the PI's academic independence for data analysis; and preservation of full academic freedoms with regard to publication rights and privileges. If funding will be from NIH (or other grant), the date on which the grant application must be noted.

j. The status of IRB approval.

k. An acknowledgment that the ChiLDReN ancillary studies policy, including the policy on publications and presentations arising from ancillary studies, applies to the ancillary study. If the AS is being supported by a non-Federal entity, then the acknowledgement must also include the flow down of the AS policy into the formal agreement and to any entity that receives ChiLDReN data or biospecimens.

l. A signed statement attesting that the proposed study has no conflict or overlap with an existing study.

m. A signed acknowledgement that the proposal investigator agrees that upon acceptance
of ChiLDReN data and/or specimens, s/he agrees to share results from his/her ancillary study with ChiLDReN upon request of the ASC.

n. Each ancillary study must have the approval of the Principal Investigator at each ChiLDReN site expecting to participate in the study. Depending on proposal type, completion of a data and/or specimen request form may be required.

o. ALL ancillary study proposals (regardless of type) should be accompanied by the biosketches of all associated investigators. Other Support pages may be requested at a later date.

The completed ancillary study proposal forms and data and specimen request forms are submitted electronically via email to ChiLDReN-ancillary@arborresearch.org.

Please see the ChiLDReN Ancillary Study Proposal Submission BRIEF Instructions provided on the members-only ChiLDReN website via the path below (you will need to log in).

Documents > Committees > Ancillary Studies Committee > Ancillary Study Forms & Admin Information

This document is also available on the ChiLDReN public website via the path below, which does not require a login.

https://childrennetwork.org/For-Collaborators

6. Processing and review of new ancillary study proposals:
   a. Once a Proposal is completed and ready for submission, proposals are submitted via email to ChiLDReN-ancillary@arborresearch.org.

   b. Proposals must be received at the email address above by the following dates (or the following business day if these dates fall on weekend or holiday):
      • January 1
      • March 1
      • May 1
      • July 1
      • September 1
      • November 1

   c. Upon receipt, the Administrative (Admin) Core, ASC Chair and SDCC will perform administrative review within 2 working days. If the proposal meets all submission requirements and does not appear to overlap with other ancillary studies (either active or under review), the Admin Core will respond to the proposing PI to inform him/her that the application has been accepted and will be reviewed, and the approximate date of the committee review. Proposals that do not pass administrative review will be returned to the submitting investigators with brief comments.

   d. Proposals that will be submitted to NIH and other federal agencies:
      ASC members will be provided with all documents associated with each submitted proposal. A Review Chair will be designated for each proposal received by the ASC. The Review Chair can be the ASC Chair or Vice Chair (in cases of multiple submissions or conflicts by the ASC Chair) or other ASC members, as needed. The Review Chair (either the ASC Chair or Vice Chair) will assign two committee members to serve as the primary reviewers of each proposal and will request that these two members provide brief written reviews following the format below. If a particular proposal requires specific expertise not represented by the committee members, the Chair can select an additional reviewer or two from among the membership of the SC. Any committee
member who proposes, collaborates on, or is from the same institution as the proposal PI, is excused from the review of that proposal. The remaining committee members will be asked to review each proposal and be prepared to discuss all proposals on a forthcoming committee call, or by email. In the case of the former, written comments to be sent to the Research Administrator and/or the committee chair from any committee member are encouraged, but are not required beyond the two designated reviewers of each proposal. In the case of the latter, an email summary or formal review is requested of each ASC member. For these proposals, written comments from designated reviewers should focus on the following:

- The overall impact and significance of the proposed study to ChiLDReN
- Strengths and weaknesses of the proposal, with particular attention to the request for specimens and/or data from ChiLDReN. Since these proposals will undergo peer review at the Federal funding agency, the committee should not review the scientific merit in great detail, but rather focus on whether this proposal would be the best use of Network specimens or data if the proposal received a fundable review from the Federal agency.
- Suggestions for improvement of the proposal should be included under the strengths and weaknesses.

All written reviews and comments should be submitted to the Research Administrator and Review Chair by a set date. The chair will then collate the review comments and summarize them for the conference call to follow. All committee members will review all proposals unless conflicted.

e. **Proposals that will be funded by funding sources other than federal agencies:**

ASC members will be provided with all documents associated with each submitted proposal. The Chair will assign two committee members to serve as the primary reviewers of each proposal and will request that these two members provide **thorough** written reviews following the format described on the “ChiLDReN Studies Review Template.” If a particular proposal requires specific expertise not represented by the committee members, the Chair can select an additional reviewer or two from among the membership of the SC. Any committee member who proposes, collaborates on, or is from the same institution as the proposal PI, may be excused from the review of that proposal. The remaining committee members will be asked to review each proposal and be prepared to discuss all proposals on a forthcoming committee call. Written comments to be sent to the committee chair from any committee member are encouraged but are not required beyond the two designated reviewers of each proposal. For these “non-federal” proposals, written comments from designated reviewers should be completed on the “ChiLDReN Studies Review Template” which will be provided with each proposal that requires full peer review by the ASC. All written reviews and comments should be submitted to the Research Administrator and Review Chair by a set date. The chair will then collate the review comments and summarize them for the conference call or email discussion to follow. All committee members will review all proposals unless conflicted.

f. **The Review Chair will lead the review of each proposal on a conference call or via email.** If the Review Chair believes a conference call is warranted, this call will occur on pre-determined dates (approximately 10 weeks before the NIH grant submission dates) to discuss each proposal and vote on approval. The PI of each proposal may be given an opportunity to join this conference call to provide a 5-minute summary of the proposal and answer questions from the committee members, though this is not always
possible. A closed session will then be conducted for further discussion of the proposal, followed by electronic voting by committee members (organized by the SDCC). If no call is held, the Review Chair can address questions directly with the proposal PI as needed and can communicate with ASC members via email about the proposal and decisions. If the proposal is to be submitted to NIH (or other federal agency) and the committee believes it has merit but is not approvable in its current form, the PI may resubmit a revised proposal (including changes suggested by the committee) within 10 business days of receipt of the Decision Letter (see below) for a second review of the proposal. This second review will be conducted by email (or by conference call if desired by a majority of the committee) and a decision sent to the PI within 10 business days of receipt. If the concerns are “substantive,” and the proposal is not approved, then the revised proposal may be submitted to the committee in the future as a new submission. If the proposal is not to be submitted to NIH for funding, then the bar for scientific review is higher and is reflected in the discussion and decision of the committee.

g. The Chair will then report on the next SC conference call or face-to-face meeting the recommendations of the ASC for approval or disapproval of each proposal reviewed in the prior session, giving a brief description of the study, the requested resources needed from ChiLDReN and a summary of the discussion. The SC will approve or disapprove the recommendations of the ASC via electronic voting organized by the SDCC. For example, if the ASC recommendation is to APPROVE with contingencies, SC members will be asked to vote YES to agree with the recommendation or NO to reject the ASC recommendation. Decisions will be based on a simple majority of the eligible votes. Sites that submitted ancillary proposals will not be allowed to vote on proposals from their own sites.

h. Following the SC vote, the Review Chair(s) will summarize the reviews, the discussion, the approved recommendations and voting results. The Chair will provide that text to the Admin Core for a letter to be sent by the Admin Core to the PI of each proposal, generally within 5 business days of approval. This letter will include directives to the proposal PI regarding the potential for expedited email review (within 10 business days) or the need for resubmission of proposals that are not approved.

i. The Admin Core will also send a follow-up message to the full SC reporting on the outcome of the vote or will verbally report updates on the next SC call.

j. PIs of approved proposals will contact the SDCC (ChiLDReN-Project-Team@arborresearch.org) to access data or specimens.

k. Any proposed amendments or minor updates to approved ancillary studies can be submitted to the ASC via email to ChiLDReN-ancillary@arborresearch.org at any time. All amendments will be reviewed by the ASC Chair/Vice-Chair for determination of further steps. Unless full committee review with discussion is deemed necessary by the Chair/Vice-Chair, reviews of amendments and updates will be handled via email communication with Committee members in an expedited manner and will be reported to the SC. A vote of the SC will not be necessary in most cases.

7. Access to data, repository specimens, and ChiLDReN resources
Access by ancillary studies to ChiLDReN specimens and data collected on participants will be governed by the ChiLDReN SC and administered by the ASC and SDCC. Upon final approval of the ancillary study proposal and acquisition of funding, the SDCC will be given the clearance to work directly with the investigator to determine the exact data and/or samples to be distributed.
It is likely that access to baseline specimens and data from a ChiLDReN clinical trial study will be allocated to an ancillary study prior to the conclusion of the ChiLDReN trial, but only after ChiLDReN SC has determined that the baseline data are of a quality suitable for sharing and that sharing them will not interfere with the completion of the trial. Follow-up specimens, data and information about treatment assignment in a clinical trial are unlikely to be available until after the trial has ended, regardless of the timing of the ancillary study. Ancillary study investigators should be aware that there may be delays of possibly years before such data are released.

ChiLDReN specimens, i.e., serum, plasma, cDNA, or DNA samples, will be provided to the ancillary study investigators after funding is secured. The study investigator (and ChiLDReN liaison, as relevant) will certify funding by submission of their signed, updated specimen request forms. Specimen analyses are to be completed, in most cases, within 12 months of receipt of the specimens.

An ancillary study may not use the central resources of ChiLDReN (e.g., SDCC) for ancillary study purposes unless such use is agreed upon by the central resource and is supported by funding from the ancillary study. The ancillary study must make its own arrangements for whatever repository, data collection, management, and analysis support that it needs. An ancillary study should not interfere with or duplicate, interfere, or compete scientifically with activities or scientific objectives of a main study (e.g. START), a sub study, an existing ancillary study, or pilot and feasibility study. ChiLDReN investigators or liaisons proposing an ancillary study will be required to sign a statement attesting that they have thoroughly reviewed all existing studies (available on the ChiLDReN website) for conflict with the proposed study and have identified none. It behooves investigators finding potential conflicts to discuss them with the ChiLDReN liaison before signing that there are none. If, after a study is completed, overlap with an existing study is identified (see Section 9 for publication requirements), permission to publish results may be denied.

8. Data sharing

8.1 Sharing of Ancillary Study Results with ChiLDReN
Specimens and clinical data are provided to the ancillary study investigator with the understanding that all data acquired and results generated through the performance of an ancillary study must be made available to ChiLDReN upon request of the ASC. While it will not be required for all ancillary study results to be shared automatically with ChiLDReN, other network investigators may submit requests for ancillary study data to the ASC. These requests will be reviewed by the process described previously in sections 5 & 6. Expedited reviews of these requests will be at the discretion of the ASC Chair. All decisions regarding these requests will be made by the ASC Chair or Vice Chair as they are submitted and within one month of the date on which the request is submitted to children-ancillary@arborresearch.org.

8.2 Progress Reports of Ongoing Ancillary Studies
A written progress report of no more than one-page length that outlines data analysis results must be provided to the ChiLDReN ASC once annually. A final report outlining study results must be sent to the ChiLDReN ASC at the completion of the project. Any
manuscripts or abstracts for professional society meetings (see section 9) resulting from usage of ChiLDReN specimens must be reviewed by the Publications and Presentations Committee and ChiLDReN must receive credit for all presentations and publications resulting from usage of ChiLDReN specimens.

9. Publications, abstracts, and presentations arising from an ancillary study

Publications and abstracts arising from ancillary studies must be reviewed by the ChiLDReN Presentations and Publications Committee prior to submission. The purpose of the review is to ensure that any statements about the ChiLDReN protocol are accurate and that the ChiLDReN resources used in the ancillary study are appropriately acknowledged. Another purpose is to be sure that no conflict or overlap with existing or ongoing approved ancillary studies or proposed publications exists.

Authorship format should be proposed by the ancillary studies writing group and will be subject to review by the Presentations and Publications Committee; the format is expected to be either conventional (with an acknowledgment of ChiLDReN) or modified conventional (author list for ChiLDReN). Ancillary study manuscripts should include an acknowledgment of the ChiLDReN investigator who served as the ancillary study liaison (if not included as a co-author in the manuscript) and the grant number for the clinical site associated with the ancillary study. Grant numbers do not have to be specified on acknowledgments for abstracts and presentations.

If during review of proposed publications overlap or conflict with ongoing ChiLDReN investigations is discovered, permission to publish will be denied. It may be possible for an author/investigator to resolve the conflict by demonstrating that the results of the study advance the field by improving upon those of existing studies (i.e. a better methodology was used). It is the purview of the ChiLDReN SC to resolve these issues and to oversee how the conflicting or overlapping results are presented in the manuscript in order to maintain the integrity of ChiLDReN.

The process for review of manuscripts will be:

a. The draft manuscript should be sent to the SDCC, on behalf of the Presentations and Publications Committee via email; ChiLDReN-Project-Team@arborresearch.org. The authors should specify the target journal or meeting.

b. For submissions with deadlines, the draft must be submitted to ChiLDReN-Project-Team@arborresearch.org at least 6 weeks before the submission deadline.

c. The chair of the Presentations and Publications Committee will identify an internal reviewer within 7 working days.

d. The reviewer will review the paper for accuracy of statements about the ChiLDReN resources used in the ancillary study, for appropriate acknowledgment of ChiLDReN, for overlap with other ChiLDReN ancillary studies or publication proposals, and for comment on any concerns about the validity of the data, its analysis, and the conclusions reached.

e. The reviewer will send his/her review to the chair of the Presentations and Publications Committee within 10 working days.

f. The result of the review may be that the manuscript or abstract is approved for submission to the NIDDK or that it needs revisions and further review.

g. The final step in the ChiLDReN internal review process is submission to NIDDK for
review within 5 working days. All papers and abstracts arising from ChiLDReN, including ancillary study reports, must be reviewed by NIDDK prior to submission. The SDCC will submit the manuscript to the NIDDK representatives after receiving approval from the Presentations and Publications Committee to do so.

g. The NIDDK project scientist will notify the Presentations and Publications Committee when the manuscript is approved for submission.

h. The SDCC, on behalf of the Presentations and Publications Committee, will notify the primary author of the decision made by the Presentations and Publications Committee (at least three days before any applicable manuscript submission deadline).

i. The SDCC supports the operations of the Presentations and Publications Committee by arranging Committee conference calls, maintaining the lists of publications studies and archiving the correspondence files relating the Committee’s activities.

j. If dispute occurs between the authors and the Presentations and Publications Committee, resolution of the dispute is the responsibility of the SC.

If a manuscript is not accepted upon initial submission to a journal, the manuscript does not need to be re-reviewed by ChiLDReN after revision and prior to resubmission to a journal, unless there have been substantive changes to the statements that relate to ChiLDReN resources or the acknowledgment of ChiLDReN. The ancillary study investigator will decide if re-review by ChiLDReN is needed.

Abstracts intended for national or international meetings (e.g., AASLD, DDW) must be reviewed by the ChiLDReN Presentations and Publications Committee.

The process for review of abstracts will be:

a. Draft abstracts should be sent to the SDCC, on behalf of the Presentations and Publications Committee ChiLDReN-Project-Team@arborresearch.org at least 3 weeks prior to the abstract submission deadline. Abstracts received after this deadline may be reviewed, if possible, but the Presentations and Publications Committee cannot guarantee to complete the review in time to meet the submission deadline.

b. The abstract will be circulated to the Presentations and Publications Committee and NIDDK (ChiLDReN-pub@arborresearch.org) for review.

c. The results of the review may be that the abstract is approved for submission, not approved for submission, or that it needs revision and second review by the Presentations and Publications Committee.

d. The SDCC, on behalf of the Presentations and Publications Committee, will notify the abstract authors of the decision made by the Presentations and Publications Committee at least five days before the abstract submission deadline.

e. Presentations (oral or poster) arising from ancillary studies will not require approval from ChiLDReN. However, ChiLDReN welcomes being informed about such presentations and would provide review of materials if requested. It is expected that any presentation from an ancillary study will include appropriate acknowledgment of the ChiLDReN resources used by the ancillary study.

10. Completion of, and closing of an ancillary study

Publication of results as intended in the ancillary study proposal is considered to be the close of the study. Once this takes place, all ChiLDReN data and remaining specimens should be managed per the instructions of the ASC and SDCC at that time. If sufficient specimens
remain to perform additional examinations or measurements, the investigator may consider using them only if the plans for additional analyses have been submitted to the ASC and approved before such studies are initiated. Please see sections 10.1 and 10.2 for more information. Any exceptions to the policies defined in Sections 10.1 and 10.2 must be approved by the ChiLDReN ASC and EC.

### 10.1. Use of, and disposal of, biological specimens provided from ChiLDReN

It is understood that specimens provided by ChiLDReN for an ancillary study are to be used only for the purpose(s) expressly detailed in the proposal. If an investigator discovers a new use for them, no matter how potentially valuable and timely to an emerging field of study, s/he must submit a new ancillary study proposal detailing the proposed use, which will undergo full review. Failure to comply with this requirement will certainly result in denial of permission to publish the results of the study.

If no plans have been approved by the ASC to extend the study or otherwise maintain Network specimens, it is the responsibility of the ancillary study investigator (and ChiLDReN liaison if the investigator is not a member of the SC) to dispose of specimens upon completion of the ancillary study for which they were acquired, if the investigators do not plan to submit a new ancillary study to extend the use of the samples. The time of completion of the study will be taken as the date of publication of the results of the study. The specimens are to be disposed of and the investigator (and liaison if applicable) will be asked to certify this in writing within 6 months of the publication date. The method of disposal should be in accordance with the biosafety committee (or similar agency) of the investigator’s institution.

In some instances, the proposed studies will not be completed (i.e. results will not be published), in which case the specimens may not be held indefinitely. A period of 2 years from the date of distribution of the specimens to the investigator or 6 months prior to the termination of the NIDDK-funded ChiLDReN Network, is taken as reasonable to complete the study. The specimens are to be disposed of and the investigator (and liaison if applicable) will be asked to certify this in writing within 2 years and 3 months of the date of specimen distribution, or 6 months prior to the termination of the NIDDK-funded ChiLDReN Network. That is unless the investigator has applied to the ChiLDReN ASC for an extension and has received approval for holding the specimens for some amount of time (to be prescribed in the application and approval, but not to exceed 2 years). The date by which specimens are to be disposed of then moves forward to 3 months after the extension date or completion of the study, whichever comes first. Investigators may not apply for a second extension.

Specimens may not be returned to the ChiLDReN repository under any circumstances. The quality of the specimens cannot be assured once they have been distributed to an entity other than the NIDDK central repositories. If for some reason the specimens have not been used, their use does not deplete them, or residuals are sufficient to perform additional studies, it is considered responsible behavior on the part of the investigator to find use for them.

Possible uses include additional studies by the investigator or studies by other investigators. Any such use is governed by ChiLDReN in the same way the primary use
has been. An application must be made for an ancillary study by the process described above. If approval is given to use the samples, ChiLDReN takes no responsibility for assuring their distribution or for their quality.

Publication of results and other activities of secondary ancillary studies are governed by ChiLDReN exactly as are activities of primary ancillary studies.

After end of the study, or 6 months prior to the termination of the NIDDK-funded ChiLDReN Network, study PIs must communicate directly with the ASC for instructions on further handling of Network specimens. The ASC, with approval of the SC, as needed, will determine if use of Network specimens can continue or if they should be destroyed. Written, signed certification of the final disposition of Network specimens will be required of each study PI upon request of the ASC. This documentation should be sent to the SDCC at ChiLDReN-Project-Team@arborresearch.org.

10.2. Use of, and destruction of, data provided from ChiLDReN

It is understood that data provided by ChiLDReN for an ancillary study are to be used only for the purpose expressly detailed in the proposal. If an investigator discovers a new use for them, no matter how potentially valuable and timely to an emerging field of study, s/he must submit a new ancillary study proposal detailing the proposed use, which will undergo full review. Failure to comply with this requirement will certainly result in denial of permission to publish the results of the study.

It is the responsibility of the ancillary study investigator (and ChiLDReN liaison if the investigator is not a member of the SC) to make good-faith efforts to permanently delete all ChiLDReN data files and associated derived electronic data files upon completion of the ancillary study for which they were acquired, or 6 months prior to the termination of the NIDDK-funded ChiLDReN Network. The time of completion of the study will be taken as 6 months from the date of publication of the primary results of the study or 6 months prior to the termination of the NIDDK-funded ChiLDReN Network. It is the responsibility of the investigator (and liaison if applicable) to certify the completion of the data file deletion and to affirm that no further use of the data for any purpose will be made. Written, signed certification of the final disposition of Network data will be required of each study PI upon request of the ASC.

If further use of the data for any purpose is desired, permission must be requested from the ASC and a new ancillary study proposal must be submitted for review not later than 3 months after publication of the primary results paper, which must be accompanied with a new Publication Proposal.

11. Miscellaneous issues

11.1. Consent and IRB issues

Consent for the ancillary study may not be part of any ChiLDReN consent – ancillary studies are separate from ChiLDReN core activities by definition. Therefore, each ancillary study must have its own consent form. Each site participating in an ancillary study must have approval from their IRB for participation in the ancillary study; or by appropriate IRB mechanism.
11.2. Funding issues
Ancillary studies are not supported by ChiLDReN resources. Investigators proposing ancillary studies must seek funding from outside sources to conduct the research. Examples include funding obtained through investigator-initiated NIH research grant awards (R01s), program announcements, grants from academic institutions, or private sources (e.g., drug companies, non-profit health organizations). The ChiLDReN SC can provide letters of support for applications for funding for approved ancillary studies. If funding is not approved, the letter of support may not be used for other applications. A revised ancillary study proposal should be submitted, and a new letter of support will be provided if the study is approved. Conduct of ancillary studies must comply with all existing ChiLDReN and NIH policies and guidelines. If the application for an ancillary study states that it is to be submitted for funding by NIH or another federal source, it is understood that the data, specimens and other resources of ChiLDReN may not be used until a Notice of Grant Award is issued. If alternative funding is identified, a revised study proposal form may be submitted that describes the funding and how it will suffice to complete the proposed studies. PLEASE NOTE: If the funding source or service is from a private party (i.e.: industry, foundation, etc..) then a formal agreement must be executed between the PI, the PI's institution, and the private party. The agreement will need to be reviewed by the NIDDK with respect to the preservation of the PI's academic independence for data analysis; and preservation of full academic freedoms with regard to publication rights and privileges.

An ancillary study wishing to use the services of the SDCC or any other ChiLDReN central resource may contact the principal investigator of that resource regarding participation in the ancillary study. Such participation has to be funded with non-ChiLDReN resources.

11.3. Expiration of ChiLDReN approval
In general, approved ancillary studies must be initiated within one year of being approved, or the approval will be withdrawn. This will allow reallocation of resources reserved for an ancillary study that does not go forward, e.g., due to failure to obtain funding, relocation of the proposing investigator, or loss of interest in the proposed research. The principal investigator of the ancillary study and the ChiLDReN SC liaison will each receive written notice 2 months before an ancillary study’s approval is due to expire. The ancillary study investigator may appeal this expiration of approval, e.g., if a funding decision is pending or if an application for funding is being revised and resubmitted. The ancillary study investigator should send a letter requesting an extension of approval to the chair of the ASC. The letter should indicate the expected timeline for initiation of the ancillary study and describe the actions that are being taken to meet that timeline.

11.4. ChiLDReN Liaison
An ancillary study that is proposed by an investigator outside of ChiLDReN must have a liaison from within ChiLDReN. This person must be a ChiLDReN SC grantee PI (the PI or corresponding PI named on the Notice of Grant Award). The liaison serves as the communications link between the SC and the ancillary study. For example, the liaison or liaison designee would provide status reports on the ancillary study at the ASC conference calls, at SC meetings, and would assist the SDCC as needed in communicating with the ancillary study investigators. The liaison may participate in the ancillary study, but participation is not required.
11.5. Changes to an ancillary study’s protocol
If a major change occurs to an ancillary study’s protocol after it has been approved (e.g.,
addition of a visit, addition of a specimen, or addition of a measurement on a specimen),
the ASC must approve the change before it is implemented. The SC will be asked to
approve the alterations, based on the recommendation of the ASC.

11.6. Confidentiality
Confidentiality of individually identifiable data about ChiLDReN participants must be
assured. ChiLDReN provides no assurances that ancillary studies will be able to identify
and contact ChiLDReN participants in the future, particularly after ChiLDReN ends.

12. Appendices
12.1. NIDDK Central Repositories Specimen and Data Use Certification

Acknowledgments:
In drafting the ChiLDReN Ancillary Studies Policy, we referred to the NASH CRN and HBRN
ancillary studies policies.