GpCRC

Gastroparesis
Clinical Research Consortium (GpCRC)

DRAFT

GpCRC
Ancillary Studies Policy

June 1, 2020

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1. Background

The Gastroparesis Clinical Research Consortium (GpCRC) studies comprise a large and well-characterized population of individuals with diabetic, surgical, and idiopathic gastroparesis. To make the best possible use of this extraordinary resource, the GpCRC encourages external investigators, as well as GpCRC investigators, to develop ancillary studies. Interested investigators must identify a member of the Steering Committee who is willing to oversee the ancillary study and serve as a liaison between the

proposer and the GpCRC Steering Committee.

2. Definition of an ancillary study

An ancillary study is defined as a study that uses GpCRC participants and/or data and biological specimens collected from them for a purpose other than intended by the GpCRC study scientific objectives as written into its protocols and procedures. In general, ancillary studies are funded by a mechanism that is separate from the GpCRC funding mechanisms. An ancillary study may require new data or biospecimen collection (i.e., additional to that required by the GpCRC) from GpCRC participants, such as a new questionnaire to complete, an additional procedure to undergo, additional blood collection, or additional biospecimens such as urine or stool. If the ancillary study places an additional burden on GpCRC participants, then a separate consent form is required as well as IRB approval. An ancillary study may involve all GpCRC participants or GpCRC participants at one or several GpCRC sites. Examples of potential GpCRC ancillary studies include proposals on pathobiology or pathophysiology of gastroparesis or collecting new symptoms, or quality of life-related data in the GpCRC population.

An ancillary study may not use the central resources of the GpCRC (e.g., GpCRC samples and data in the NIDDK Central Repository, the GpCRC digital repository data stored at the Scientific Data Research Center (SDRC), SDRC data management resources, or SDRC analysis resources) for ancillary study purposes unless such use is agreed upon by the central resource and is entirely supported by 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 significantly overlap with activities of a main study (e.g., GpR, GpR 2, GpR 3, PGpR, NORIG, GLUMIT-DG, APRON, PBG, PQLGM, or BESST), a substudy, an existing ancillary study, or a pilot and feasibility study. GpCRC 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 GpCRC website) for conflict with the proposed study and have identified no conflicts. It behooves investigators and liaisons to find potential conflicts before signing that there are none. If overlap with an existing approved ancillary study is identified, permission to publish all or part of the results from the later ancillary study may be denied.

An ancillary study will be considered complete when the primary results paper for each aim has been accepted for publication. If the approved timelines for completion of the ancillary study are not met (see sections 8, 9 and 10), a formal request justifying continuation of the ancillary study must be approved by the Steering Committee.

3. Ancillary studies policy and procedures

The ancillary studies policy includes the following:

- To review applications for ancillary studies of the GpCRC and to make recommendations for approval or disapproval
- To maintain a list of all proposed ancillary studies indicating approval status and the liaison. For approved studies, the list will indicate initiation date and the GpCRC centers participating in the ancillary study.
- To maintain a list of allocations or commitments of existing or future GpCRC samples to central GpCRC and to ancillary studies.

The list of all proposed ancillary studies and the list of allocations and commitments of existing or future GpCRC samples will be available on the GpCRC website.

With respect to votes on matters decided by the Steering Committee, each Steering Committee member has one vote. In case of a tie vote, the Steering Committee will decide by mailed ballot if a meeting or conference call is not needed.

If a Steering Committee member proposes an ancillary study, collaborates on an ancillary study, or is affiliated with the institution of an investigator who proposes an ancillary study, he/she will be excused from reviewing and voting on that ancillary study proposal, similar to NIH peer review policies for avoidance of actual or perceived conflicts of interest.

The SDRC supports the ancillary studies operations by arranging conference calls, receiving submitted applications for ancillary studies, administering the process for review of submitted applications, writing correspondence for the Steering Committee, and maintaining the lists of ancillary studies and allocated/committed samples and the document and correspondence files relating the Committee's activities. The SDRC relies on the named liaison for each ancillary study and the Steering Committee members in completion of these activities.

4. Proposing an ancillary study

Investigators wishing to conduct an ancillary study must complete a GpCRC Ancillary Study Proposal (SP) application. The SP form is available on the open part of the GpCRC website (www.gpcrc.us), click on Ancillary Studies, then Ancillary Study Proposal (SP form). Completed SP forms are submitted to the Steering Committee in care of the SDRC. Submission of electronically completed PDF forms is preferred over faxed forms for ease of reading; typing the investigator's and liaison's names instead of actual signatures is adequate.

The deadlines for receipt of ancillary study proposals for review by the GpCRC Steering Committee are 1 February, 1 June, and 1 October. Proposals received by 1 February of each year will be reviewed and the proposer notified of the decision by 31 March. Similarly, proposals received by 1 June will be reviewed and the proposer notified by 31 July, and proposals received by 1 October will be reviewed and the proposer notified by 30 November. These receipt dates allow notification of the applicant of the GpCRC Steering Committee's approval or disapproval approximately two months before the NIH due dates for funding applications for new projects.

An ancillary study that is proposed by an investigator outside of the GpCRC must have a GpCRC liaison. This person must be a GpCRC Steering Committee member. The liaison serves as the communications link between the Steering Committee and the ancillary study. For example, the liaison would provide status reports on the ancillary study as needed at Steering Committee meetings and would assist the Data Coordinating Center as needed in communicating with the ancillary study. The liaison may participate in the ancillary study but participation is not required. A link to a listing of GpCRC Steering Committee members is in the Appendix (section 14).

Investigators who are responding to a program announcement or applying for funding should gain GpCRC Steering Committee approval for the ancillary study **before** submitting their application to a funding organization.

Completion of the Ancillary Studies proposal requires the following information:

- Name of the principal investigator for the ancillary study, his/her institutional affiliation and contact information.
- Name of the GpCRC Steering Committee member liaison, his/her institutional affiliation and contact information.
- Names of other key investigators for the ancillary study and their institutional affiliations.
- Assurance that all study investigators have reviewed the proposal and agreed to participate **prior** to submission of the proposal to the Steering Committee.
- The study title, objective, and estimated start and end dates.
- A concept sheet describing the research design and methods for achieving the study objectives (2- page maximum length - this is to be a concise, well organized description).
- The primary outcome variable and sample size, with justification.
- Specification of the GpCRC resources which the ancillary study wishes to use:
  - If access to previously collected specimens is required for new measurements, then the quantity and amount of specimens to be used per participant, study and visit must be specified. Note that if exactly 0.5 mL of serum or plasma is needed to run the planned assays, then two aliquots should be requested per participant-study-visit, or the number of assays reduced. Any conditions of specimen collection (e.g., green-top sodium heparin collected blood) must be specified.
  - Number of participants involved.
  - Description of new data or measurements that are to be collected on enrolled or future GpCRC participants or specimens.
  - If new specimens will be collected, then the quantity of specimens to be collected from participants and the conditions of specimen collection must be specified.
  - Frequency of visits or number of participant contacts for collection of new data or specimens.
  - Types of interview questions, physical measures, or data to be collected from participants.
  - If access to previously collected GpCRC clinical data is requested (e.g., demographics, previously collected measures on specimens, treatment information), the data items must be specified.
- The funding source, funding amount, and status of funding for the ancillary study. Any work or personnel time expected of the GpCRC SDRC, investigators or staff that is not reimbursed by the ancillary study must be specified so that the Steering Committee can evaluate whether the GpCRC should assume that unreimbursed work or personnel time or if there will be a fee for the work to be performed.
- If the funding is being provided through a collaboration with industry or another NIH agency (designated as the ancillary study's Collaboration Partner), then the ancillary study's GpCRC liaison must have a Collaborative Partner Agreement between their institution and the Collaboration Partner, and NIDDK must approve the completed Agreement prior to its execution. The link to the GpCRC Partner Collaboration Agreement template is included in the Appendix (section 14).
- The status of IRB approval, if separate IRB approval is required, and plans and procedures to

protect participant confidentiality.

- An acknowledgment that the GpCRC Ancillary Studies Policy and the policy on presentations and publications arising from ancillary studies have been read and will be abided by the study principal investigator.
- A signed statement attesting that the proposed study has no conflict or overlap with existing studies.
- The date of the expected completion of the assay/genotyping results or other new data once biospecimens have been received, and the anticipated date of completion of analysis if the study's analysis is performed outside the SDRC.
- Any time-sensitive dates for consideration of receipt of biosamples from the NIDDK Biorepository or clinical data from the SDRC should be designated by the GpCRC liaison.

Each ancillary study must have the approval of the Principal Investigator at each GpCRC clinical center which will participate in the study.

The ancillary study activities that use GpCRC resources may not proceed until the GpCRC Steering Committee has approved the ancillary study and proof of funding has been received at the SDRC.

5. Review process for proposed ancillary studies

The SDRC will circulate the submitted ancillary study proposal (SP form) to the members of the Steering Committee with instructions that they are to send their comments to the SDRC by a specified date, typically one week before the meeting or conference call at which it will be discussed. The SDRC will assist the Chair to collate the comments and prepare a written memo to the Steering Committee specifying the recommendation for approval or disapproval. The Steering Committee will review that recommendation at their next meeting or conference call and decide for approval or disapproval. The principal investigator of the ancillary study and the GpCRC Steering Committee liaison will each receive a copy of the memo directing the Steering Committee to review the study application (so that they know the time frame for review) and a copy of the memo from the Steering Committee specifying the decision for approval or disapproval.

Steering Committee members and other reviewers will be asked to assess:

- Whether the study has sufficient scientific merit
- Whether the study has sufficient power
- Whether the study would interfere with other GpCRC activities
- Whether the study would hamper continued recruitment or participation in the GpCRC
- Whether the study is consistent with the GpCRC aim of facilitating a broad range of research relevant to gastroparesis
- Whether the biosample request is justified by the scientific merit of the study
- Whether the volume of requested biospecimens is justified in consideration of other requests for this resource by GpCRC investigators
- Whether they recommend approval or disapproval of the study
- In addition, the SDRC will provide an estimate of the availability of the resource or whether the resource is adequate for the study request

6. Funding issues

Ancillary studies must be supported from non-GpCRC resources. Investigators proposing ancillary studies should seek funding from outside sources to conduct their research. Examples of funding sources include investigator-initiated NIH research grant awards (R01s), NIH program funding awards, grants from local academic institutions or private sources (e.g., drug companies, non-profit health organizations), etc. The GpCRC Steering Committee can provide letters of support for applications for funding for ancillary studies approved by the GpCRC. If funding is not approved, the letter of support may not be used for other applications. A revised ancillary study proposal or amendment should be submitted to the SDRC and a new letter of support will be provided. Conduct of ancillary studies must comply with all existing GpCRC and NIDDK/NIH policies and guidelines.

If the ancillary study applied for funding by NIH or another federal source, any requested GpCRC data, specimens, and other resources will not be provided until a Notice of Grant Award is issued. If alternative funding is identified, an amendment or revised study proposal form may be submitted that describes the funding and how it will suffice to complete the proposed study.

Services provided by the SDRC or other GpCRC central resource may require payment so as not to draw on existing funding for the GpCRC. Payment for these services must be funded with non-GpCRC resources. The investigator may be responsible for costs to the SDRC for sample selection, preparation of datasets, and analysis support and advice. Costs, if any, to the SDRC or other central resource will depend on the extent of the proposed work, the amount of time estimated to complete the work, and whether the study fulfills a proposed aim of the GpCRC. The GpCRC SDRC Director and the GpCRC study liaison, with oversight from the NIDDK GpCRC Program Official, will determine whether a fee will be charged and the details.

In addition, the study's primary investigator will be responsible for any costs charged by the NIDDK Central Repositories to aliquot, pull, package, and ship requested biosamples. See Appendix (section 14) for NIDDK Central Repositories costs.

7. Consent and IRB issues

Consent for the ancillary study cannot be part of any GpCRC consent – ancillary studies are separate from the GpCRC by definition. Therefore, each ancillary study must have its own consent form if needed. Each center participating in an ancillary study must have approval from their IRB for participation in the ancillary study.

7. IRB compliance and proper use of biological specimens and clinical data

The GpCRC liaison to the ancillary study is responsible for ensuring that all uses of any GpCRC biospecimens or clinical data provided to the ancillary study are in accordance with the consent statements signed by the GpCRC study participants. Some ancillary studies will require IRB approvals and participant consent statements. The GpCRC liaison to the ancillary study is responsible for informing the Steering Committee (via the SDRC) of IRB submissions, amendments, and annual renewals.

Specimens and clinical data provided by the GpCRC for an ancillary study must only be used for the approved aims specified in the ancillary study proposal. Any new aims will require either an ancillary study amendment or a new ancillary study proposal. Additional information concerning amendments is provided in section 13.2. Misuse of the biological specimens or clinical data provided by the GpCRC is a serious breach of academic trust. Consequences will be determined with input from the Steering Committee and the NIDDK.

8. GpCRC general guidelines for access to and use of biological specimens and clinical data

Access by ancillary studies to GpCRC biospecimens and data collected on participants will be governed by the GpCRC Steering Committee and administered by the SDRC. Biospecimens and corresponding clinical data **are not provided simultaneously**; biospecimens are provided first, and the clinical data will be supplied by the GpCRC SDRC at the time of, or after, completion and receipt of data from the ancillary study. If the ancillary study investigator has requested baseline biospecimens and data from a GpCRC clinical trial or a study that is still in recruitment and/or follow-up phase, the Steering Committee must approve the data/specimen sharing timeline. Otherwise, biospecimens and data will be provided for approved ancillary studies once the GpCRC study or trial is either complete or the SDRC has determined that the baseline or follow-up data are of a quality suitable for sharing, and that the quantity of biospecimens requested does not interfere with the GpCRC study's aims. Follow-up specimens and associated data and information about treatment assignment in a GpCRC clinical trial are unlikely to be available until after the GpCRC trial has ended and the primary paper from the GpCRC trial has been accepted for publication, regardless of the timing of the submission of the ancillary study. Ancillary study investigators should be aware that there may be delays of possibly years before the requested GpCRC specimens or data are approved for release to an ancillary study liaison.

GpCRC data sets use the GpCRC Patient ID number to link patient records. Ancillary study investigators should request data on the GpCRC participants in their study by providing the GpCRC ID numbers of the patients whose data are requested. The SDRC will accept SAS, Excel, Access, ASCII, and other data files of records of GpCRC ID numbers (word processing files are not acceptable, other identifiers are not acceptable). The GpCRC data which have been approved for provision to the ancillary study will be provided in SAS data sets using whatever SAS version is in use at the SDRC. Ancillary study investigators should be prepared to deal with SAS data sets.

The samples and data collected using GpCRC central resources belong to the GpCRC. The GpCRC samples and data are provided to the ancillary study liaison with the understanding that all new data (e.g., biomarker and genomic data) generated through the ancillary study will be shared with other GpCRC investigators once the primary paper for the primary aim of the ancillary study is accepted for publication. Other GpCRC investigators may request approval from the ancillary study's liaison for access to a subset of the ancillary study-generated data prior to the SDRC release date of the complete ancillary study-generated data file for inclusion in: 1) a GpCRC manuscript or 2) another ancillary study's analysis. Inclusion of these data will be specified on the publication proposal or ancillary study proposal, which will require review and approval by the Steering Committee (see section 10.3).

The GpCRC must be granted access to all datasets acquired during the performance of an approved ancillary study prior to presentation or publication of results and upon request.

The clinical dataset will be provided by the GpCRC SDRC at the time of, or after completion and receipt of the generated new data (e.g., genomic, proteomic measures) from the ancillary study. The specified timeline for the receipt of the clinical dataset in relation to the return of the new data should be included in the study proposal, with justification of any special arrangements requested, such as a "new data/clinical data" simultaneous exchange, and approved by the Steering Committee. Additional information is provided in Sections 10.2 and 10.3.

9. GpCRC Biospecimens

9.1. Access to GpCRC Biospecimens

The GpCRC biospecimens, e.g., serum, plasma, gastric tissue, or DNA samples, will be provided to the ancillary study's liaison only if the following conditions are agreed to in writing by the ancillary study liaison's institution:

1) The necessary funding support and availability of staff and equipment to generate the new data are secured and ready to start the ancillary study within 6 months of receipt of the specimens.

2) The new data derived from the ancillary study must be completed within 27 months of receipt of the specimens, or 3 months prior to the termination date of the GpCRC final grant funding cycle.

3) Any new data generated by the ancillary study must be sent to the SDRC or to an approved designated digital repository **prior to the release** of the clinical dataset by the SDRC. Alternatively, the Ancillary Studies Committee/ Steering Committee, and the NIDDK Program Official may approve special arrangements for the provision of the new data with respect to the release by the SDRC of the associated clinical data. Arrangements must be included in the ancillary study proposal and/or in the Collaborative Partner Agreement. The NIDDK will oversee the terms of the agreement.

4) The ancillary study's liaison and principal investigator must read the Data Sharing requirements designated in the GpCRC Ancillary Studies Policy and provide assurance to abide by these requirements.

9.2. Disposal of biospecimens remaining at the end of the ancillary study

It is the responsibility of the GpCRC liaison for the ancillary study to arrange for proper disposal of any remaining GpCRC biospecimens after completion of all of the ancillary study aims. Once the ancillary study aims are met, the GpCRC liaison must submit a plan and timeline for destruction or other disposition of the remaining biospecimens. The plan and timeline must be approved by the Steering Committee. Documentation confirming the disposal in accordance with the approved plan must be submitted to the SDRC within one month of disposal if the ancillary study liaison does not plan to submit an amendment or a new ancillary study proposal to extend the use of the samples.

Biospecimens received from the NIDDK Biorepository may be kept for a period of up to 5 years from

receipt of specimens or up to 3 months prior to the termination date of the final GpCRC grant funding cycle, whichever comes first. Retention of biospecimens allows execution of rigor and reproducibility requirements and for potential future GpCRC approved analysis done conjointly only with the GpCRC. Specimens must be disposed of within 3 months of these dates in accordance with the biosafety committee (or similar agency) of the investigator's institution and meet all local requirements of the institution. Certification of specimen disposal must be provided in writing by the ancillary study investigator and the GpCRC liaison.

If the primary results of each of the aims of the ancillary study have not been published within 5 years of receipt of the biospecimens, or the termination of the GpCRC (whichever comes first), then the investigator may request permission from the Steering Committee to extend retention of the specimens and to dispose of the specimens at a future date once all aims of the ancillary study have been published. A progress report and proposed timeline for publication will be submitted to the Steering Committee along with the written request. The GpCRC liaison will be responsible for the oversight of the unused biosamples to ensure that the samples are only used for the GpCRC proposed purpose, and destroyed in accordance with local institutional guidelines.

Specimens cannot be returned to the NIDDK Biosample repository. If, for some reason, the specimens have not been used or are not depleted, and residuals are sufficient to perform additional studies, it is desirable and responsible behavior on the part of the ancillary study liaison and primary 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 the GpCRC in the same way the primary use has been governed. Application must be made for an ancillary study amendment or new proposal by the process described in sections 4 and 13.2. If approval is given to use the remainder of the samples, the GPCRC takes no responsibility for assuring their distribution or for their quality. Publication of results and other activities of secondary ancillary studies are governed by the GpCRC exactly as are activities of primary ancillary studies.

9.3. Disposal of GpCRC biospecimens at the end of GpCRC funding

All biosamples provided by the GpCRC for an ancillary study remaining at the end of the final GpCRC funding period must be disposed of 3 months prior to the termination of the GpCRC as stated in section 9.2. Documentation of biospecimen disposal must be provided via email to the SDRC. The ancillary study liaison will be responsible for assuring the destruction of the biospecimens.

Any biosamples belonging to the GpCRC remaining in the NIDDK Biosample Repository will be documented by the SDRC using a random identification number and become available for public use through the NIDDK Central Repository website. The NIDDK Central Repository will provide oversight for the use of these samples, requiring an approved NIDDK Central Repositories Sample and Data Use Certification (SDUC) agreement and a Research Plan for the proposed study and use of biosamples (see Appendix, section 14).

10. Data sharing

10.1. Provision of the ancillary study data to the GpCRC

The ancillary study investigator or the GpCRC Steering Committee member serving as the liaison between the GpCRC and the ancillary study are responsible for providing data files including new data (raw or processed) obtained from an ancillary study such as biomarkers measured in GpCRC serum, plasma samples or genomic data generated from GpCRC DNA samples. GpCRC specimens, i.e., serum, plasma, DNA samples, will be provided to the ancillary study investigators under the condition that funding and analytical capabilities are secured to start the ancillary study within three months and, analyses must be completed within six months of receipt of the specimens. Assay results or data obtained from the ancillary study analyses will be made available within one year of completion to the GpCRC for incorporation into the database for use by other investigators. GpCRC clinical information on study participants will be provided to the ancillary study investigator or liaison after all raw or processed data generated through the ancillary study are returned to the GpCRC SDRC. Any data (raw or processed) provided to conduct an approved ancillary study may only be used in the manner in which the Steering Committee & NIDDK has approved (see Section 9 Appendices, for the template NIDDK Central Repositories & Data Use Certification documents).

A written progress report must be provided to the GpCRC every six months which outlines data analysis results. A final report outlining study results must be sent to the GpCRC SC at the completion of the project. Any manuscripts resulting from usage of GpCRC specimens must be reviewed by the Steering Committee and GpCRC must receive credit for all presentations and publications resulting from usage of the GpCRC specimens.

Data and samples collected using GpCRC central resources are overseen by the NIDDK; these are GpCRC data and GpCRC samples. Data and samples collected from GpCRC patients under an approved ancillary study protocol and using ancillary study resources are overseen by the ancillary study investigators. Measurements made on GpCRC samples under an approved ancillary study protocol and paid for by ancillary study resources are also overseen by the ancillary study investigators and will be incorporated into the GpCRC database.

10.2. Provision of GpCRC clinical data to ancillary study liaison

Once the ancillary study has completed generating new data on any GPCRC biospecimens provided to the ancillary study and has deposited those new data with the GPCRC or approved other digital repository, the SDRC will provide the GPCRC clinical data agreed to in the approved Ancillary Study proposal to the ancillary study liaison and to the designated investigator at a collaborating institution. Any designated collaborative investigator is determined by the GPCRC liaison and must be approved by the Ancillary Studies Committee and the NIDDK GPCRC Program Officer.

Any new data (raw, processed, or collected) derived by the ancillary study through use of GPCRC biospecimens or any GPCRC clinical data provided to ancillary study investigators **may only be used** in the manner specified in the approved GPCRC Ancillary Studies proposal or in the approved Collaborative Partner Agreement. Any uses not in the approved proposal are subject to prior review and approval of an amended ancillary study proposal. The ancillary study investigators must also comply with applicable data use requirements of the NIDDK and the GPCRC (see Appendix, section 14, for the template NIDDK Central Repositories Sample and Data Use Certification and the GPCRC Data Protection Assurance agreements). It will be considered scientific misconduct to use the new data or the shared clinical data from GPCRC for any purpose other than the purposes specified in the ancillary study proposal aims.

10.3. Sharing of ancillary study data deposited with the GPCRC

Data that are generated from ancillary studies, such as assay results or genomic data, must be deposited with the GPCRC. These data may be shared with the GPCRC investigators once the ancillary study's primary aim has been accepted for publication. However, with express permission by the GPCRC liaison to the ancillary study, along with the ancillary study's principal investigator, the newly-generated data may be released sooner for an approved GPCRC publication proposal or for use in another approved ancillary study proposal. The new ancillary study proposal or publication proposal using the new data may not overlap with any other approved ancillary study aim or publication proposal aim. If the study-generated data are used for a new GPCRC abstract or publication, the ancillary study principal investigator and the GPCRC liaison will be invited to join the writing committee and included as co-coauthors.

10.4. Use and destruction of data provided from the GPCRC SDRC

Clinical data provided by the GPCRC for an ancillary study must only be used for the purpose expressly detailed in the proposal or in the Collaborative Partner Agreement. If an investigator discovers a new use for the data, no matter how potentially valuable and timely to an emerging field of study, the liaison must submit either an amendment or a new ancillary study proposal detailing the proposed new use. The amendment or new proposal will undergo full review by the Ancillary Studies Committee. Failure to comply with this requirement will constitute a breach of scientific conduct. The GPCRC Steering Committee with the NIDDK Program Official will decide on remediation, such as denial of permission to publish the abstract or manuscript or other editorial remedies, such as reporting the breach to the journal and/or to the investigator's institution. Further, no further use of the clinical data will be permitted, and assurance that the clinical dataset has been destroyed will be required.

It is the responsibility of the GPCRC liaison in collaboration with the ancillary study principal investigator to make a good-faith effort to permanently delete all GPCRC data files and associated derived electronic data files upon completion of each of the ancillary study aims for which they were acquired. The ancillary study is considered complete when the primary results manuscript is accepted for publication for each of the approved ancillary study aims. Data must be deleted within 2 years of publication acceptance for the last ancillary study aim. Documentation confirming the deletion of all data files must be sent to the SDRC within one month of deletion by the GPCRC ancillary study liaison.

Investigators may request an extension to keep the clinical data for a longer period of time if needed to complete all approved aims. A written request, including the reason for the extension, must be submitted by the ancillary study liaison to the Ancillary Studies Committee for review and approval. The request must include an assurance that the clinical data will not be used for any purpose other than those specified in the approved Ancillary Study proposal and, if applicable, in the Collaborative Partner Agreement. Any other use of the clinical data for new purposes is prohibited.

For approved extensions that go beyond the termination date of the final GPCRC grant project funding cycle, the GPCRC liaison will become the designated Data Custodian for continued approved uses of the GPCRC data. The designated Data Custodian will provide assurance that the principal collaborative investigator may continue to use but not share the dataset for the approved aims. Any publications arising from the additional aims after the termination of the GPCRC must acknowledge the

GPCRC investigators via the Credit Roster and also invite the ancillary study liaison and the ancillary study's investigators to be included in the writing committee as co-authors and reviewers. In the case that the GPCRC liaison can no longer be the designated Data Custodian, then he may designate another co-author who is or was also a GPCRC Steering Committee member.

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

Publications arising from ancillary studies do not need to be approved by the GpCRC Steering Committee prior to initiation. However, publications arising from ancillary studies must be reviewed by the GpCRC Steering Committee prior to journal submission; the purpose of the review is to assure that any statements about the GpCRC study protocol are accurate and that the GpCRC resources used in the ancillary study are appropriately acknowledged.

11.1 Publications

The following steps must be completed prior to submitting an ancillary studies manuscript to a journal:

- The draft manuscript should be sent to the Steering Committee in care of the SDRC; the authors should specify the target journal.
- The paper will be circulated to the Steering Committee for voluntary comment directed to the corresponding author.
- The Chair will identify an internal reviewer for the paper and send the paper to that individual with a deadline for response.
- The reviewer will review the paper for accuracy of statements about the GpCRC resources used in the ancillary study and for appropriate acknowledgment of the GpCRC.
- The reviewer will send his/her review to the Chair.
- The result of the review may be that the manuscript is approved for submission to the NIDDK or that the manuscript needs revisions and further review.
- The final step in the GpCRC internal review process is submission to NIDDK for review. All papers arising from the GpCRC, including ancillary study reports must be reviewed by NIDDK prior to journal submission. The proposing investigator will submit the manuscript to the NIDDK project scientist after receiving approval from the Steering Committee to do so.
- The NIDDK project scientist will notify the proposing investigator (with a copy to the SDRC) when the manuscript is approved for journal submission.

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

11.2 Abstracts and presentations

Abstracts and presentations arising from ancillary studies will not require approval from the GpCRC. However, the GpCRC 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 GpCRC resources used by the ancillary study.

11.3 Authorship

Authorship for publications and presentations from ancillary studies is at the discretion of the ancillary study investigators. It is expected that conventional authorship will be used, with an acknowledgment of the GpCRC.

12. Progress reports

The SDRC will query the study investigators and the study liaison of active ancillary studies for a status update semi-annually. Additionally, the ancillary study liaison is responsible for the applicable timely deposits of the ancillary study data to the appropriate public use digital repository (e.g., genomic data results submitted to dbGaP).

13. Miscellaneous issues

13.1. Failure to initiate the ancillary study

In general, approved ancillary studies must be initiated within one year of being approved, or the approval will be withdrawn; this will allow recycling of resources allocated to an ancillary study that does not go forward, (e.g., due to failure to obtain funding). The principal investigator of the ancillary study and the GpCRC 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 GpCRC 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 Steering Committee. 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.

13.2. Amendments to an approved ancillary study research plan

If a major change occurs to an approved ancillary study's research plan, the ancillary study liaison must submit an email to the Steering Committee describing and justifying the amendment. Changes to an approved ancillary study may include a request for additional samples, adding additional ancillary study aims in alignment with the overall objective of the ancillary study, a change to the Research Plan to use a different method of ascertaining the new data, or a substantive change in the analysis plan. Approval of amendments requires approval by vote of the Steering Committee.

13.3. Postings to the GpCRC website

- Ancillary study meeting dates and proposal due dates for each meeting.

- All study proposals (initial, revisions), reviews, decisions from the Steering Committee, and any other material pertinent to the history of the Ancillary Study will be posted on the closed portion of the Ancillary Studies website.
- Final versions of GpCRC manuscripts arising from an approved Ancillary Study will be posted on the password-protected GpCRC website Publications page.

Acknowledgments:
This policy is based on the ancillary studies policy developed by the GPCRC; and in drafting the GPCRC Ancillary Studies Policy, we referred to the following sources: Ancillary Studies policies of the NASH CRN, Virahep-C, HALT-C, BARC, and CLiC studies sponsored by the NIDDK, and the National Emphysema Treatment Trial sponsored by the NHLBI.

14. Appendix

- GPCRC Ancillary Study Proposal form
- NIDDK Central Repositories Specimen and Data Use Certification
- GpCRC Steering Committee liaisons
- Process to obtain samples from the NIDDK Biorepository
- GpCRC Collaborative Partner Agreement template
- Cost of retrieving samples from the NIDDK Central Repositories
- GpCRC Data Use Assurance Protection agreement