Diabetic Foot Consortium

Ancillary Studies Policy and Procedures

Version 1.0
Approved by Steering Committee 17June2022

Contents

1 Background

The Diabetic Foot Consortium (DFC) studies include well-characterized populations of individuals with diabetic foot ulcers for whom data are collected and stored by the Data Coordinating Center (DCC) and biological samples are processed and stored at local clinical research units, biomarker analysis units (BAUs), the DFC Central Laboratory, and in the NIDDK Central Repository. To make the best possible use of this extraordinary resource, the DFC Steering Committee encourages investigators, both internal and external to the consortium 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 DFC participants and/or data and/or biological specimens collected for research not included in the active DFC protocols, procedures and analysis. In general, ancillary studies are characterized as being outside the specific scientific objectives of the DFC 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 DFC 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 DFC protocols and case report forms) from participants, such as a new questionnaire to complete, or a new biologic specimen to be obtained from participants. An ancillary study may involve all DFC participants of a certain type or class or participants at a subset of DFC clinical research units.

3 Function of the Ancillary Studies Committee

The Ancillary Studies Committee is under the direction of the DFC Executive Committee. Additional input and guidance may be sought from the DFC Steering Committee.

The DCC supports the operations of the Ancillary Studies Committee by maintaining the DFC Ancillary Studies website page; receiving submitted applications for ancillary studies, administering the process for review of submitted applications, writing correspondence for the Committee, notifying the Steering Committee of voting results, and providing an overview of the Ancillary Studies to the OSMB.

The DCC will document and store all Ancillary Study Proposal approvals/disapprovals and all status updates. The DCC supports the operations of the Ancillary Studies Committee 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 is charged with facilitating the use of DFC resources to achieve the greatest scientific benefit possible, providing feedback to potential ancillary investigator(s) regarding the suitability of the ancillary protocol for integration into the DFC and its likelihood of approval by the Steering Committee. To do this, the committee considers several important factors in each proposal.

- **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 diabetic foot ulcers and/or what gaps in knowledge will be closed by the research.

- **Justification of the burden being placed on DFC**. By definition, all ancillary studies will use DFC infrastructure and/or resources. If those resources are not exhaustible, such as electronically stored data, then the burden is minimal, the cost of providing the resource minimal, and the justification for their use not critical. If they are scarce and non-renewable (e.g., wound biopsy specimens), then 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., additional burdens placed on patients 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.
- **Feasibility.** For studies requesting existing data and/or biosamples, a preliminary review will determine if the DFC can provide the requested data and number and types of biosamples. For studies requesting additional data and biosamples collection, a preliminary review will determine if the DFC can fulfill the request in a reasonable time given the DFC knowledge of the participants, ongoing protocols and clinical site resources.
- **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.
- **Plans for funding.** Ancillary studies are approved based on adequate funding to complete the research. If an applicant is applying for funding for the Ancillary Study, the final approval will be contingent on guaranteed funding. The Committee will write a letter in support of a grant application stating that the samples being requested are available to the investigator if the grant is funded within a reasonable time and will be stated in the Letter of Support. Investigators 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. 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 (e.g., industry, foundation), 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.
- **Conflict or major scientific overlap with another study.** Conflict is apparent in several ways. One likely conflict 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 DFC objectives will not be approved.

4 Composition, Structure, and Operations of the Ancillary Studies Committee

4.1 Ancillary Studies Committee Membership

The Ancillary Studies Committee is comprised of members from each of the Clinical Research Units, the DCC and the NIDDK as follows:

- One Chairperson (PI or Co-I from a DFC clinical research unit)
- One Vice-Chairperson (PI or Co-I from a clinical research unit)
- One DCC representative
- One NIDDK representative
- At least one coordinator
- At least one representative from each Clinical research unit
- Biorepository Committee chair or delegate
- Project Manager (from DCC; non-voting member)

There are no term limits; however, at the start of each grant cycle, the membership and leadership of the Ancillary Studies Committee will be assessed. If a Chair steps down prior to the end of the grant cycle, the vice chair will become the chair. The vice-chair will be selected from the Ancillary Study Committee membership, with endorsement by the DFC Steering Committee.

4.2 Ancillary Studies Committee Operations

The Ancillary Studies Committee will meet monthly by email and/or conference call to review and vote on all proposals received in a given review period.

Ancillary proposals will be accepted on a rolling basis. Applications should be submitted at least eight weeks prior to the grant submission deadline to allow for review by the Ancillary Studies Committee and final decision by the DFC Steering Committee. Submissions must be received at least one week in advance of the monthly Ancillary Studies Committee meeting (second Wednesday of each month) in order to initiate review that month.

At least half of the members of the Ancillary Studies Committee constitutes a quorum for endorsing a recommendation that will be sent to the Steering Committee for their vote. After endorsement by the DFC Steering Committee, the DCC will notify the proposal PI of the DFC's decision.

5 Proposing an ancillary study

Any investigator in the DFC, whether a clinical research unit PI or a Co-investigator, may submit an ancillary study proposal. Any other investigator (i.e., from outside of a DFC center or working within a DFC center but not a named investigator) wishing to conduct an ancillary study must be sponsored by a member of the DFC (a list of DFC members is on the DFC website, http://diabeticfootconsortium.org/). By giving their endorsement, a DFC member agrees to be the Liaison between the investigator and DFC and to be responsible for ensuring that all DFC policies are met.

If a DFC PI is an active participant or co-investigator in the ancillary study, it is appropriate that he/she submit the proposal.

The DFC Ancillary Study Application Forms, including the DFC ANCILLARY STUDY PROPOSAL FORM, the DFC DATA REQUEST FORM, and the DFC BIOREPOSITORY SPECIMEN REQUEST FORM, are available on the DFC public website http://diabeticfootconsortium.org/ under the Information for Collaborators tab. A DFC Ancillary Study Data Use and Material Transfer Agreement (Appendix 13.1) must be in place prior to the release of DFC samples.

5.1 Feasibility determination

To determine the feasibility of the proposed ancillary study, it is required that the proposal PI and DFC Liaison (see section 12.4 below) who is contemplating submission of an ancillary study to the DFC (prior to full submission to the Ancillary Studies Committee) should review the DFC website for (1) the list of consortium and active ancillary studies for any potential overlap between the proposed study and other studies within DFC; (2) the current protocols that include the data, imaging and biosample collection and study timeline; and (3) the Central Laboratory list of sample types, amounts and collection procedures. It is expected that the proposal PI (if a DFC member) or a DFC Liaison (if not) will ensure that the proposal is feasible and will attest to this by signing the DFC ANCILLARY STUDY PROPOSAL FORM prior to its submission to the Ancillary Studies Committee.

5.2 Completion of Ancillary Study Application Forms

After the proposal PI (if a DFC member) or a DFC Liaison (if not) ensures that the proposal is feasible, the following should be submitted on the Ancillary Study application forms. The proposal should not exceed 5 pages, excluding references and biosketches.

a. Study title
b. The principal investigator (PI) for the ancillary study and his/her institutional affiliation.
c. Names of other key investigators for the ancillary study and their institutional affiliations
d. Name of the sponsoring DFC member (for non-DFC applicants)
e. Planned start and end dates
f. Funding source and status of funding for the ancillary study (including grant number, if applicable).
g. Estimated costs for the DCC, clinical sites and Central Laboratory.
h. Design and methods
    - Statement of primary and secondary goals and objectives
    - Brief background, significance, and rationale
    - Hypothesis and specific aims
    - Study design and procedures
        - Define the study patient population (inclusion and exclusion criteria)
        - Describe plan for data acquisition
        - Describe sample collection and handling
        - Describe specific assays and experiments proposed
        - Describe planned quality control measures
        - Define main outcome measures
    - Sample size and justification (including power calculation)

- Plans for analysis (For each study aim, describe the plan(s) for data analysis, the specific hypothesis that the statistical method will test/estimate, how controls will be included, is the goal for estimation vs. hypothesis testing)
- Anticipated results and study timeline
- Describe plan for obtaining IRB approval (if needed)
- Description of additional methods and procedures to be carried out on a study participant and the rationale for those methods and procedures
- Burden on participants
- Measures to be taken to ensure participant safety and confidentiality
- Payment or incentives to participants
- Data requested from the DFC central database, or from additional tests, procedures, surveys, etc.
- Biomaterial requested
- Describe the DFC study clinical centers involvement
- Describe the DCC Data Coordinating Center involvement
- References

i. An acknowledgment that the DFC Ancillary Studies policy, including the policy on publications and presentations arising from ancillary studies, applies to the ancillary study. If the ancillary study is being supported by a non-federal entity, then the acknowledgement must also include the flow down of the Ancillary Studies policy into the formal agreement and to any entity that receives DFC data or biospecimens. This acknowledgment is provided in the DFC ANCILLARY STUDY PROPOSAL FORM.
j. Depending on proposal type, completion of a data and/or specimen request form may be required.
k. 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 are submitted electronically via email to DFC-Ancillary@umich.edu, and data and specimen request forms are submitted electronically via email to DFC-DCC-PM@umich.edu.

6 Processing and review of new ancillary study proposals:

Upon receipt of completed ancillary study proposals forms and data and specimen requests forms, the DCC Project Manager, Ancillary Studies Committee Chair and DCC 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 DCC Project Manager will respond to the proposing PI to inform them 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.

Ancillary Studies Committee 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. 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 Steering Committee. 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 proposals, written comments from designated reviewers should be completed on the "Ancillary Study Evaluation Form" which will be provided with each proposal that requires full peer review by the Ancillary Studies Committee. All written reviews and comments should be submitted to the DCC Project Manager 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.

a. 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 review will occur at the regular monthly ASC meeting. 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 DCC). If no call is held, the Review Chair can address questions directly with the proposal PI as needed and can communicate with Ancillary Studies Committee members via email about the proposal and decisions.

b. 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 re-submit 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.

c. The Ancillary Studies Chair will then report, via email, to the DFC Steering the recommendations of the Ancillary Studies Committee for voting on each proposal reviewed, giving a brief description of the study, the investigator, and the Ancillary Studies Committee recommendation. The DFC Steering Committee will (1) approve, (2) disapprove, (3) abstain, or (4) request a discussion of the proposal at its next Steering Committee meeting via electronic voting organized by the DCC. For example, if the Ancillary Studies Committee recommendation is to APPROVE with contingencies, Steering Committee members may vote YES to agree with the recommendation or NO to reject the Ancillary Studies Committee recommendation. Decisions will be based on a simple majority of the eligible votes. Clinical research units that submitted ancillary proposals will not be allowed to vote on proposals from their own clinical research units.

d. Following the DFC Steering Committee vote, the DCC will tally the vote and provide the results to the DFC Ancillary Studies Committee and the Steering Committee. The Review Chair(s) will summarize the reviews, the discussion, the approved recommendations and voting results. The Chair will provide that text to the DCC Project Manager for a letter to be sent to the PI of each proposal, generally within 5 business days of approval.

e. PIs of approved proposals will contact the DCC (DFC-DCC-PM@umich.edu) to access data or specimens.

f. Any proposed amendments or minor updates to approved ancillary studies can be submitted to the Ancillary Studies Committee via email to DFC-Ancillary@umich.edu at any time. All amendments will be reviewed by the Ancillary Studies Committee Chair or Vice-Chair for determination of further steps. Unless full committee review with discussion is deemed necessary by the Chair or 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 Steering Committee. A vote of the Steering Committee will not be necessary in most cases.

6.1 NIDDK approval

If the funding source or service is from a private party (e.g., industry, foundation), 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. In addition, the DFC Ancillary Study Data Use and Material Transfer Agreement (see Appendix 13.1) must be completed.

If funding will be from NIH (or other grant), the date on which the grant application must be noted. For internal DFC sites, the DFC Ancillary Study Data` Use and Material Transfer Agreement (see Appendix 13.1) does not need to be completed.

7 Access to data, repository specimens, and DFC resources

Access by ancillary studies to DFC specimens and data collected on participants will be governed by the DFC Steering Committee and administered by the Ancillary Studies Committee and DCC. Upon final approval of the ancillary study proposal and acquisition of funding, the DCC 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 DFC study will be allocated to an ancillary study prior to the conclusion of the DFC study, but only after the DFC Steering Committee 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 study. Follow-up specimens, data and information about treatment assignment in a clinical trial (if applicable) 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.

DFC specimens (e.g., serum, plasma, tissue, or wound dressings) will be provided to the ancillary study investigators after funding is secured. Quality assessments of requested biospecimens may be requested from the Biorepository Committee separately. The study investigator (and DFC 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 the DFC (e.g., DCC or BAU) 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. If, after a study is completed, overlap with an existing study is identified (see Section 10 for publication requirements), permission to publish results may be denied.

8 Human Subjects and Data Confidentiality

Confidentiality of DFC participants must be guaranteed. Individually identifiable data will not be released. Per the DFC Ancillary Study Data Use and Material Transfer Agreement, no attempt shall be made to link subject data to a DFC participant.

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 DFC studies.

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

The ancillary study investigator must provide a copy of the IRB approval or exemption letter prior to release of data or samples. 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 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 DFC DCC.

9 Data sharing

The DFC policy and procedure for data sharing conforms to the NIH Data Sharing Policy (current version remains in effect until January 25, 2023, at which time it will be replaced; see NOT-OD-21-013 Final NIH Policy for Data Management and Sharing).

9.1 Sharing of ancillary study results with DFC

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 DFC at the completion of the ancillary study.

Other consortium investigators may submit requests for ancillary study data to the Ancillary Studies Committee. These requests will be reviewed by the process described previously in sections 5 & 6.

9.2 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 DFC Ancillary Studies Committee at least once annually, with the option of providing an oral presentation to the Committee, upon request. A final report outlining study results must be sent to the DFC Ancillary Studies Committee at the completion of the project. At the completion of the ancillary study, the investigator will present their results to the Steering Committee. Any manuscripts, abstracts or presentations for professional society meetings resulting from usage of DFC specimens must be reviewed by the Publications and Presentations Committee and DFC must receive credit for all presentations and publications resulting from usage of DFC specimens and data.

10 Publications, abstracts, and presentations arising from an ancillary study

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

11 Completion and closing of an ancillary study

Six months after publication of results as intended in the ancillary study proposal is considered to be the close of the study, or 6 months prior to the termination of the NIDDK-funded DFC, if this occurs earlier. Once this takes place, all DFC data and remaining specimens should be managed per the instructions of the Biorepository Committee, Ancillary Studies Committee and DCC at that time.

11.1 Use of, and disposal of, biological specimens provided from DFC

It is understood that specimens provided by DFC 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 sufficient specimens remain to perform additional examinations or measurements at the close of the ancillary study, the investigator may consider using them only if the plans for additional analyses have been submitted to the Ancillary Studies Committee not later than 3 months after publication of the primary results paper and approved before such studies are initiated.

After the end of the study, or 6 months prior to the termination of the NIDDK-funded DFC, ancillary study PIs must communicate directly with the Ancillary Studies Committee for instructions on further handling of Consortium specimens.

All efforts should be made to not destroy DFC biospecimens; however, specimens may not be held indefinitely at the institution of the ancillary study investigator. If the Ancillary Studies Committee determines, based on the progress report that the ancillary study is unlikely to be completed in a timely fashion (e.g., investigator changes institutions) or no publications will result from the study, it will notify the DFC Biorepository Committee. A period of 6 months prior to the termination of the NIDDK-funded DFC is taken as reasonable to complete the study.

When the Biorepository Committee has been notified by the Ancillary Study that the ancillary study is completed or is unlikely to be completed and there are unused biospecimens at the institution of the ancillary study investigator, they will determine the future status of the biospecimens. The Biorepository Committee, with approval of the Steering Committee, as needed, will determine if use of Consortium specimens can continue or if they should be destroyed. Possible options include:

(1) Shipping the biospecimens to the DFC Central Laboratory or NIDDK Central Repository, or

(2) Requesting the ancillary study PIs dispose of the biospecimens. If no plans have been approved by the Ancillary Studies Committee to extend the study or by the Biorepository Committee to retain Consortium specimens, it is the responsibility of the ancillary study investigator (and DFC liaison if the investigator is not a member of the Consortium) to dispose of the specimens upon completion of the ancillary study for which they were acquired and to certify this in writing within 6 months of the publication date or the date of communication with the Biorepository Committee. The method of disposal should be in accordance with the biosafety committee (or similar agency) of the investigator's institution.

Written, signed certification of the final disposition of Consortium specimens will be required of each ancillary study PI who receives DFC biosamples. This documentation should be sent to the DCC at DFC-DCC-PM@umich.edu.

11.2 Use of, and destruction of, data provided from DFC

It is understood that data provided by the DFC 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 a 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 DFC liaison if the investigator is not a member of the Steering Committee) to make good-faith efforts to permanently delete all DFC data files and associated derived electronic data files upon completion of the ancillary study for which they were acquired. The time of completion of the study will be taken as the earlier of 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 DFC. It is the responsibility of the investigator (and liaison if applicable) to certify the completion of the data file(s) 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 Consortium data will be required of each study PI.

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

12 Miscellaneous issues

12.1 Consent and IRB issues

An ancillary study may require an additional consent form if the research is not covered by the consent form that was used to collect the requested biosamples and data. If a new consent form is required, each clinical research unit participating in an ancillary study must have approval from their IRB for participation in the ancillary study, or by appropriate IRB mechanism.

12.2 Funding issues

Ancillary studies are not supported by DFC resources. Investigators proposing ancillary studies must seek funding from outside sources to conduct the research. The DFC Steering Committee will 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 DFC 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 DFC 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 (e.g., industry, foundation), please see Section 6.1.

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

12.3 Expiration of DFC 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 DFC 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 Ancillary Studies 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.

12.4 DFC Liaison

An ancillary study that is proposed by an investigator outside of DFC must have a liaison from within DFC. This person must be a DFC DCC or clinical site PI or co-I. The liaison serves as the communications link between the Steering Committee and the ancillary study. For example, the liaison or liaison designee would provide status reports on the ancillary study at the Ancillary Studies Committee conference calls, at Steering Committee meetings, and

would assist the DCC as needed in communicating with the ancillary study investigators. The liaison may participate in the ancillary study, but participation is not required.

12.5 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 Ancillary Studies Committee must approve the change before it is implemented. The Steering Committee will be asked to approve the alterations, based on the recommendation of the Ancillary Studies Committee.

13 Appendices

13.1 DFC Ancillary Study Data Use and Material Transfer Agreement

DFC 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, Room 1034, Ann Arbor, MI 48109 ("Provider"), acting as the Data Coordinating Center ("DCC") for the Diabetic Foot Consortium ("DFC"), 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").

DFC is a consortium funded by the National Institute of Diabetics and Digestive and Kidney Diseases ("NIDDK"), an institute of the National Institutes of Health ("NIH"), and therefore all applicable NIH data and samples sharing policies in regard to Material as defined, will apply.

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 activity (the "Research") that has been reviewed by the DFC Ancillary Committee ("ASC") and approved by the DFC Steering Committee ("SC").

2. The transfer of the Material constitutes permission 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 "DFC Ancillary Studies Policy and Procedures" (incorporated herein as Appendix A). Uses of the Material beyond those indicated in the Research plan require submission of an amendment for review and approval to the ASC 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. 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.

7. Recipient shall establish appropriate safeguards to ensure that the Material is used or disclosed only in compliance with the terms of this Agreement, “DFC Ancillary studies Policy and Procedures” and with all applicable statutes and regulations, including all applicable NIH policies and regulations pertaining to research with recombinant DNA that is applicable to the Material.

8. Recipient agrees, in accordance with the “DFC Ancillary Policy and Procedures”, to provide Provider with copies of all data generated by Recipient’s Research, including all data generated from the use of the Material under Recipient’s Research plan. Recipient and Scientist agree that such generated all data will be maintained by the DCC and made available to DFC participant sites and other requesting third parties.

9. This Agreement is not assignable.

10. This Agreement is effective when signed by an authorized representative of Recipient and shall terminate when all of the Material provided by Provider to Recipient is destroyed or returned to Provider. If it is infeasible to return or destroy the Material, adequate protections will be applied after they had been reviewed and approved by Provider.

WHEREFORE, the Recipient, through its authorized representative, hereby agrees to the terms of this Agreement.

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

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: _____

14 Acknowledgments

In drafting the DFC Ancillary Studies Policy, we referred to the NIDDK ChiLDReN and NEPTUNE ancillary studies policies.