11. POLICIES

It is understood by all collaborating investigators that the data collected in the HAPO Follow-Up Study are the property of the Study as a whole rather than any individual(s). This study is certain to catalyze great interest in examining associations between maternal glucose levels during pregnancy and secondary outcomes or characteristics of the population(s) as well as many ancillary studies.

11.1 Informed Consent

Although countries have different requirements for the Institutional Review Board (IRB) or Ethics Panel and informed consent process, because the HAPO Follow-Up Study is funded by the NIH, the Study is obligated to follow the policies and requirements of the Office for Protection from Research Risks (OPRR), an agency of the US government. Therefore, each time the Protocol is revised or an ancillary study added, the change must be approved by the local IRB before it can be implemented. In addition, annual IRB review and an approval letter are required. Each consent form will include the elements of informed consent as required by Title 45 in the Code of Federal Regulations.

Each mother is to have the objectives and the procedures of the HAPO Follow-Up Study explained to her, in particular, the methods of data collection (i.e., questionnaires; mother and child blood samples for glucose, insulin/C-peptide, A1c, lipids, and storage, and hsCRP in the child; measurement of blood pressure, height, weight, waist circumference, and other anthropometric measurements in mother and child from the BOD POD; and child pubertal assessment. The mother should also be told that all data collected will remain completely confidential. She is then to be asked to sign an informed consent form if she agrees to participate along with her child in the HAPO Follow-Up Study. Consent is given separately for collection of a blood sample for DNA.

Each field center IRB or Ethics Panel will have its own policy as to whether it is necessary for the child to sign an Assent Form. Whether or not a signed Assent Form is required, the study should be explained to the child in language that the child can understand and which has been approved by the IRB or Ethics Panel.

If participation is to be sought for any ancillary studies, the relevant separate ancillary study consent form should be used. Consent for any ancillary study, which must be described as optional, is only to be sought after the mother and child have consented to the HAPO Follow-up Study. Consent for the HAPO Follow-Up Study is the first priority. Those mothers who agree to participate in the HAPO Follow-Up Study but do not agree to an ancillary study are to remain as HAPO Follow-Up Study participants.

11.2 Training

All field center personnel participating in the HAPO Follow-Up Study must be trained in HAPO Follow-Up Study procedures, either during Central Training or by the field center PI or Research Nurse/Coordinator following Central Training. Only trained field center staff will be allowed to participate in data collection for the HAPO Follow-Up Study.

11.3 Privacy of Records

Data collected from individual participants are to be entered into REDCap (Research Electronic Data Capture), a secure web-based software package for data entry and management, without name and identified only by the original HAPO ID. Blood samples sent to the LCC are also to be so identified. Only local field center investigators and field center staff are to have the names of participants. The need for protecting confidentiality of these names will be stressed during Central Training as well as in the Manual of Operations.

11.4 Field Center Data Access

At the end of data collection, cleaned and corrected data from individual field centers will be made available to local investigators. Papers based on these data are not to be published prior to the main reports of the HAPO Follow-Up Study.

11.5 Publications and Presentations

It is understood by all collaborating investigators that the data collected in the HAPO Follow-Up Study are the property of the Study as a whole rather than any individual(s).

11.5.1 Main Final Paper(s)

These are to be prepared under the supervision of the Coordinating Centers and the Steering Committee. They will also be circulated to all field center investigators. Field center investigators may be members of the writing group for any paper. Authorship is to be the HAPO Follow-Up Study Cooperative Research Group, with acknowledgement of Principal Investigators, Coordinating Centers, Central Laboratory, Steering Committee, and NIH project scientists.

11.5.2 Other Study-Wide Papers

Other papers using combined study data are to be drafted by ad hoc groups of local and/or central investigators appointed by the Steering Committee. The topics of such papers may be suggested by the Coordinating Centers, Steering Committee, or local investigators. Such papers are to be authored by the investigators drafting the paper on behalf of the HAPO Follow-Up Study Cooperative Research Group, with acknowledgement also of Principal Investigators, etc. These draft papers are to be reviewed first by the Executive Committee and then by the Steering Committee.

11.5.3 Local Papers

At the end of data collection, cleaned and corrected data from individual field centers are to be made available to local investigators. Local papers are not to be published prior to publication of the main reports of the HAPO Follow-Up Study Cooperative Research Group. Output from data analyses not performed by the Data Coordinating Center must be provided to the Data Coordinating Center for review and verification along with the proposed presentation or manuscript. Local papers must also be submitted to the Steering Committee for approval.

11.6 Ancillary Studies Policies

11.6.1 General Policy

To enhance the value of the HAPO Follow-up Study, the Steering Committee welcomes proposals from individual investigators to carry out ancillary studies. Nevertheless, to protect the integrity of the HAPO Follow-up Study, ancillary studies must be reviewed and approved by

the Executive Committee, the Steering Committee, and the Observational Study Monitoring Board (OSMB) before their inception or submission of a proposal to an external funding agency.

11.6.2 Definition of an Ancillary Study

An ancillary study is defined as research or data collection involving study participants or specimens, using any technique, procedure, questionnaire or observation other than those set forth in the HAPO Follow-Up Study Protocol. Ancillary studies may be submitted by investigators participating in the HAPO Follow-up Study, or by investigators who are not part of the HAPO Follow-up Study. However, ancillary studies submitted by investigators who are not part of the HAPO Follow-up Study Cooperative Research Group must include at least one Co-Investigator who is a HAPO Follow-up Study Investigator.

No field center will be required to participate in an ancillary study that involves additional data collection or additional blood samples. Field centers not involved in a specific ancillary study at one of more field centers are encouraged to consult with the Principal Investigator of an approved study to determine if there is mutual interest in having additional field centers participate.

Ancillary studies require external funding. Examples include studies funded by NIH research awards, grants from academic institutions or private sources (e.g. private foundations, pharmaceutical companies). Any ancillary study must have sufficient funding to cover the costs incurred by the HAPO Follow-up Study Field Centers, Laboratory Coordinating Center (e.g. to process shipments and ship samples), and by the Data Coordinating Center (for tasks such as sample selection, preparing and documenting analysis files, participating in statistical analysis, and integrating the new ancillary data back into a combined database). Funds are not available for these purposes within the HAPO Follow-up Study budget. The anticipated source of funds must always be identified in the Ancillary Study Proposal.

11.6.3 Requirements and Procedures for Approval of an Ancillary Study

11.6.3.1 Overview

Participation in, and approval of an ancillary study, is subject to review and formal approval by the HAPO Follow-up Study Executive Committee, Steering Committee, and the OSMB. Concerns about a proposal will be discussed with the applicant and opportunities for clarification will be provided. An ancillary study must receive approval before grant funding is requested from an external funding agency. Investigators are encouraged to discuss potential proposals with the HAPO Follow-up Study PI, Dr. Boyd Metzger, before submitting a proposal.

11.6.3.2 Considerations for Approval

- *The proposed study must meet requirements of the highest scientific merit.*
- *Relevance to the HAPO Follow-up Study.*
- *Opportunity for acquisition of new scientific knowledge.*
- *Adequacy of experimental design, methodology and data analysis.*
- *Adequacy of the investigator and research environment.*
- *Participant (enrolled participants and field centers) burden.*
- *The proposed study must be acceptable to the participants (e.g. time, discomfort, privacy) if it involves collection of additional data or blood samples.*
- *The proposed study must not interfere with other parts of the main HAPO Follow-up Study.*
- *The proposed study must put minimal demand on scarce HAPO Follow-up Study resources such as backup blood samples.*
- *The proposed study must require the unique characteristics of the HAPO Follow-up Study participants to accomplish its goals.*
- *The investigators must have adequate resources to effectively complete the project, including both financial support and personnel.*
- *The ancillary study investigators must agree to return the complete ancillary data set back to the Data Coordinating Center, if requested.*
- *The proposed study must not interfere with or impede the completion of the primary or secondary objectives of the HAPO Follow-up Study.*
- *The proposed study must not adversely affect participant cooperation or compliance with the HAPO Follow-up Study protocol.*
- *The proposed study must not create a serious diversion of study resources (personnel,*

- *equipment or study samples) or investigator/staff time at the Field Centers or Coordinating Centers.*

11.6.3.3 IRB Review of Local Ancillary Studies

Ancillary studies proposed by individual field centers must first be approved by the local Institutional Review Board. Ancillary studies are to provide an additional local consent form, describing in detail procedures to be performed, and possible risks and benefits to the participant. Participation in the ancillary study must be described as optional. Consent for the optional study is only to be sought after the mother and child have consented to the HAPO Follow-up Study. Consent for the HAPO Follow-Up Study is the first priority. Those mothers who agree to participate in the HAPO Follow-Up Study but do not agree to an ancillary study are to remain as HAPO Follow-Up Study participants. These documents and the completed HAPO form (Ancillary Study Approval Request Form) requesting approval must be submitted to Dr. Lynn Lowe for preliminary review by the Coordinating Centers, and approved by the Executive Committee, the Steering Committee, and the OSMB prior to the start of data collection for the ancillary study.

***Note:** 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 HAPO Follow-up Study Data Coordinating Center.*

11.6.3.4 Instructions for Completion of the Ancillary Study Proposal Form

All proposed ancillary studies must be reviewed and approved by the HAPO Follow-up Study Executive Committee, Steering Committee, and OSMB before submission to a funding agency. To request approval of an ancillary study, investigators must submit a completed Ancillary Study Approval Request Form. The Ancillary Study Request Form must include the following:

1. *Title of the proposed study*
2. *Name(s) and address(es) of the Principal Investigator(s) seeking approval*
3. *Name(s) and address(es) of participating HAPO Follow-up Study investigators. If the Principal Investigator is not a HAPO Follow-up Study investigator, there must be at least one HAPO Follow-up Study Investigator included as a Co-Investigator.*

4. *Description of the goals of the proposed ancillary study and the hypothesis or hypotheses to be tested, including an overview of the literature and the background and significance pertaining to the goals and hypotheses*

5. *Description of the data to be collected, and the methods that will be used to collect the data. If the study involves additional blood samples, indicate what will be measured in each sample, and the proposed laboratory for the assays. Also, provide the volume for each sample, and the time the blood sample or samples will be collected in relation to the OGTT blood draws.*

6. *Listing of what HAPO Study and HAPO Follow-Up Study core data are required as part of the ancillary study, and the need for any other study resources*

7. *Power analysis justifying the number of participants to be included*

8. *A description of when the ancillary study data are to be collected. (Indicate also whether the data could be collected at the end of the period of data collection for each HAPO Follow-Up Study participant.)*

9. *A statement Indicating where the data analyses are to be done and the statistical methods that will be used*

10. *Identification of funding source(s) for the ancillary study*

11. *Attachment of any proposed questionnaires or forms to be used*

12. *Attachment of an abbreviated (one-two page) curriculum vitae or biographical sketch for the Principal Investigator*

13. *In accordance with common practice in ethical research worldwide, there must be local review by an independent body of your local research plans* ***including ancillary studies****. The resultant assurance, based on their review on safeguarding and protecting the rights and welfare of the human subjects in your center, is to be included with a copy of the Ancillary Study Approval Request Form. Any procedures beyond the already approved HAPO Follow-Up Study procedures must be included in a new consent form. A copy of that form is to be included together with the request for approval of the ancillary study.*

The investigator should send the Ancillary Study Approval Request Form to Dr. Lynn Lowe, the HAPO Follow-up Study Project Manager.

To ensure that the ancillary study proposal includes all the required elements, it will undergo preliminary review by members of the Executive Committee in Chicago before being submitted to the full Executive Committee for review and approval. Any concerns about a proposal at this stage will be discussed with the applicant and opportunities for clarification provided, if the proposal ~~is~~ appears likely to be approved with the additional clarifications. Once a proposal is considered complete, it will be submitted to the full Executive Committee for review and approval. Again, any concerns will be discussed with the applicant and opportunities for clarification and changes provided, as appropriate. Following review and approval by the Executive Committee, the proposal will be submitted to the Steering Committee for approval. Once the proposal has been approved by the Executive Committee and the Steering Committee, it will be submitted to the OSMB for approval.

Note: *Final approval for a proposed ancillary study rests with the OSMB. Ancillary studies not approved by the OSMB cannot be conducted.*

11.6.3.5 Changes to an Approved Ancillary Study

Once an ancillary study is approved, if a change occurs in the structure or concept of the study, such changes should be disclosed to the HAPO Follow-up Study Executive Committee for review and approval. If deemed necessary, changes may be forwarded to the OSMB for review and approval as well.

11.6.3.6 Ancillary Proposal Budget

The investigator applying for an ancillary study must supply all additional funds needed to complete the study. Provision of funds for expenses incurred by the HAPO Follow-up Study is essential. Once a study concept is approved, ancillary studies are expected to collaborate with the Coordinating Centers to develop a budget, which adequately provides for expenses incurred by the HAPO Follow-up Study. Such costs include, but are not limited to:

- *Statistical and data management staff for coordinating the additional data management and analyses with the Data Coordinating Center*

- *Costs incurred by participating Field Centers including space, personnel, equipment, and IRB approval*

- *Costs relative to visits outside of the HAPO Follow-up Study protocol*

The Principal Investigator of an ancillary study will be responsible for providing written progress reports on the ancillary study.

11.6.4 Ancillary Study Papers

Presentation and publication of the results of an ancillary study are subject to the same guidelines as apply to all other presentations and publications of HAPO, i.e., prior review and approval by the Steering Committee, before submission of an abstract for a meeting, before presentation of an oral report or poster to a meeting, and before submission to a journal.

Collaborating investigators in ancillary studies are to prepare papers in cooperation with the Clinical and Data Coordinating Centers. Output from data analyses not performed by the Data Coordinating Center must be provided to the Data Coordinating Center for review and verification along with the proposed presentation or manuscript. The final text must be approved by the Steering Committee before it is submitted for presentation and/or publication. Authorship is to be the investigators concerned, on behalf of the HAPO Follow-Up Study Cooperative Research Group.

11.7 Data Sharing

Northwestern University is committed to the open and timely dissemination of research outcomes. Participants in the HAPO Follow-Up Study will be asked to provide informed consent for the sharing of their data (including biospecimens) with other investigators. For those participants providing informed consent for data sharing, we will make de-identified study biospecimens and data available following publication of all primary results from the study to the general community by providing it to the NIDDK for their biospecimen and data repositories. The Coordinating Centers have experience with preparing data, biospecimens, and documentation for archiving and will work with repository personnel to provide these as required. Data will be provided to NIDDK in SAS datasets or other format compatible with their

repository, along with copies of data collection forms and documentation of original and derived data.