10. QUALITY CONTROL

10.1 Introduction

Uniformity of study methods and laboratory procedures are essential to the success of the HAPO Follow-Up Study. The geographic distribution of the 10 participating field centers assures ethnic/racial and socioeconomic diversity of the study population and worldwide applicability of the findings; however, it introduces a number of challenges to obtaining the maximal possible uniformity of methods and procedures. These include language barriers as well as cultural differences.

The following steps are being taken in the HAPO Follow-Up Study to assure standardized procedures throughout:

- A common Protocol and Manual of Operations (MOO) are to guide all field work.
- Central training of field center personnel responsible for field work and oversight of local data entry are a requirement for field center participation.
- A Laboratory Coordinating Center is to measure key metabolic variables (glucose, insulin/C-peptide, lipids, A1c on mothers and children and hsCRP on children only); blood specimens must be shipped to the Laboratory Coordinating Center under specified conditions for preservation.
- Standard equipment and supplies are to be used, with delivery organized by the Coordinating Centers.
- Common centrally prepared data collection forms are to be used. For foreign centers, where English is not the principal language, questionnaires administered to participants must be translated into the local language. Translated forms must be submitted to the Data Coordinating Center, prior to use, for back-translation to English to check for uniformity of meaning. In addition, instructions for participants are also to be translated and back-translated to assure uniformity of meaning.

Procedures to assess and enhance accuracy, i.e., quality control, are critical to study success. For the HAPO Follow-Up Study, these include:

- Use of trained staff members to collect all data.
- Dry Run of all procedures, except the child OGTT, before the start of actual data collection, with sufficient time for central review and any needed correction prior to start of field work; start of participant recruitment based on Executive Committee and Coordinating Center authorization.
- ~~Use of blind duplicate~~ *Random selection of 5% of participants to have their backup* samples analyzed to assess technical error of laboratory analyses and overall integrity of sample collection, processing and analysis.
- Entry on all forms of ID of staff member performing specific procedure or task.
- System for checking accuracy of the participant ID code on all forms and blood samples.
- Timely review and editing of all forms locally prior to data entry for completeness, etc.
- Entry locally of all data forms using REDCap (Research Electronic Data Capture), a secure web-based software package for data management, via high speed Internet connection and corresponding manual (see Chapter 9) prepared by the Data Coordinating Center, with appropriate range, logic, and consistency checks, and re-entry of forms containing key data.
- Defined procedures for the Data Coordinating Center and Laboratory Coordinating Center for timely monitoring of data quality, including rapid edit procedures in the Data Coordinating Center of all data, with rapid feedback to field centers, and the Laboratory Coordinating Center as necessary.
- Site visits during the Dry Run with onsite review with the field center PI (or his/her designee) of all data collection procedures for Dry Run participants; site visit reports prepared for review by the Executive and Steering Committees.
- Additional site visits during field work as necessary.
- Retraining of field center staff as needed based on ongoing quality control procedures.

10.2 Standardized Central Training

Extensive training of field center personnel in use of this manual is to occur prior to the start of local data collection. Training will consist of lectures, slide presentations, and practical sessions, as well as individual consultations. Training will cover all aspects of the study, including: recruitment and informed consent; use of HAPO participant IDs and record keeping; child visit procedures; child blood pressure, height, waist and mid-arm circumference, skinfolds and use of the BOD POD for weight and other anthropometric measurements; pubertal

assessment; maternal visit procedures; maternal blood pressure, height, waist and hip circumference, and use of the BOD POD for weight and other anthropometric measurements; drawing, processing, storage, and shipping of blood specimens; use of REDCap for data entry and data management; data editing; roles of field center PIs; and ethical issues. Training will take place in face to face sessions conducted by the Coordinating Centers in Chicago prior to beginning recruitment of participants at the individual field centers. A package of training materials will also be prepared and distributed to each field center.

10.3 Dry Run

Each field center must carry out a Dry Run (test run) of all study procedures, except the child OGTT, prior to start of actual fieldwork. The Dry Run will be conducted approximately 4-8 weeks after the completion of Central Training, and sooner if feasible. Field centers are expected to practice HAPO Follow-Up Study procedures during the interim, and to train any additional local staff who will be participating in the follow-up study.

During the Dry Run, HAPO Follow-Up Study research staff will complete data collection procedures on 3-4 mothers and children. Each field center will be site visited during the Dry Run by Coordinating Center personnel, with a site visit report prepared for review by the Executive and Steering Committees. Special Dry Run shipping labels will be prepared by the Data Coordinating Center for use by the field center during the Dry Run. All Dry Run documents and entered data will be sent to the Data Coordinating Center for quick review. Fieldwork will begin following the Dry Run after all procedures have been certified as acceptable.

The readiness of a field center to begin field work will be determined by the Executive Committee.

Only staff members certified as ready, after the above review, are to carry out HAPO Follow-Up Study procedures.

The Dry Run is a test, an opportunity to assess what has been learned and what still needs to be learned in carrying out HAPO Follow-Up Study procedures, in a standardized, high quality manner.

10.3.1 Preparation for the Dry Run

A great deal needs to be prepared for each field center's Dry Run. Background information that should be prepared includes the following:

- Prepare any material you plan to use to invite participation in the HAPO Follow-Up Study, which is to be reviewed by the Coordinating Centers. Also, have current copies of your Consent Forms available.
- Prepare a list of any other studies being conducted at the field center that could potentially make a woman or her child ineligible for participation in the HAPO Follow-Up Study.
- Prepare a description of where the child and maternal visits will be performed, including how the visits will be arranged or scheduled, and how appointments will be tracked.
- Determine what laboratory results will be considered abnormal based on local standards, how findings considered abnormal will be reported to participants, and what steps will be taken on behalf of the participant with abnormal findings.

Specific steps that should be taken to prepare for data collection during the Dry Run include the following:

- Separate Dry Run ID numbers and labels will be prepared for each center's use. File folders are to be prepared locally for "participants" examined in the Dry Run.
- All needed forms are to be duplicated and Dry Run form labels affixed to each page of each labeled form, and to the "participant" folder.
- Forms are placed in the appropriate "participant" folder, together with the Dry Run laboratory labels used later.
- All material and equipment needed for the Dry Run (and field work) are to be in place. This includes the most recent Manual of Operations.
- Extra backup equipment is to be on hand (e.g., backup power for freezers or alternate energy equipment).
- Local facilities for the maternal and child exams are to be set up. It is clearly preferable to have the Dry Run visits take place in the same locations that will be used for field work.
- Arrangements for shipment of blood and urine samples to the Laboratory Coordinating Center are to be made well before the Dry Run.

- Necessary shipping supplies are to be on hand – appropriate shipping box, cryovial boxes, appropriate forms, etc. A source for dry ice should also have been identified.

After all of these preparatory steps have been made, the field center should carry out as many practice visits and/or measurements as necessary to prepare for good performance during the Dry Run.

10.3.2 Dry Run Procedures

All examination visit procedures should be demonstrated by the field center during the Dry Run site visit.

- Blood and urine samples are to be obtained from Dry Run "participants" and processed locally and shipped to the Laboratory Coordinating Center in Chicago as spelled out in this Manual. This allows all phases of blood drawing, handling, processing, aliquot preparation, and shipping to be reviewed.
- The Laboratory Coordinating Center should be notified by e-mail of details of the Dry Run shipment of blood and urine samples.
- Data from the Dry Run are to be entered into the HAPO Follow-Up Study REDCap data base, which will then be compiled as SAS data files by the Data Coordinating Center for review and further processing. All data forms should also be copied and the originals sent to Chicago. Blood and urine samples are to be processed locally and sent to Chicago.

Final review and certification will take place after evaluation of all Dry Run material and after receipt of a satisfactory response to all problems noted by staff and central observers.

10.4 Site Visits

The HAPO Follow-Up Study Protocol includes provision for site visits to each field center by Coordinating Center staff during the Dry Run, as noted above, and during ongoing fieldwork as required based on field center performance.

Reports will be prepared for site visits that occur during each field center's Dry Run and for site visits that result from less than optimal performance by a field center. Such reports will be

reviewed by the Executive Committee (and by the Steering Committee if there are outstanding issues).

Courtesy site visits, i.e., those that are not related to the Dry Run or to a field center's performance, do not require that a report be prepared for review.

10.5 Quality Control of Physical Measurements

10.5.1 Blood Pressure

To ensure the accuracy of the blood pressure measurements throughout the Study, quality control measures are developed centrally and applied at all field centers. These measures include:

- Recruitment of the most qualified personnel as HAPO Follow-Up Study staff members.
- Comparison measurements with both electronic devices on 4 persons each month (see Section **10.5.1.1** below).

10.5.1.1 Procedure for Comparison Blood Pressure Measurements:

Each month comparison blood pressure measurements are to be obtained on 4 separate persons with results recorded on the Blood Pressure Quality Assurance Form. Comparison measurements are obtained by measuring the blood pressure using both of the Omron 705 electronic machines. Because the first of a series of blood pressure measurements tends to be higher than second or third measurements, on 2 persons the machine designated as "A" is used for the first and second measurements, and the machine designated as "B" is used for the first and second measurements, and machine "A" is used for the third measurement. The 4 second and third blood pressures measured with each machine are then averaged and compared to assess comparability of readings with the 2 machines.

The specific procedure for obtaining comparison measurements on 4 volunteers is as follows:

1. Attach the Omron A cuff to the first volunteer's right arm and let the volunteer sit quietly with feet on the floor for 5 minutes.
2. After waiting 5 minutes, take and record the measurement on the Blood Pressure Quality Assurance Form.
3. After waiting 1 minute, take a second measurement with the Omron A machine and record the measurement on the Blood Pressure Quality Assurance Form.
4. Remove the Omron A cuff and attach the Omron B cuff to the first volunteer's right arm. Wait 1 minute and then take and record the measurement on the Blood Pressure Quality Assurance Form.
5. Attach the Omron B cuff to the second volunteer's right arm. After waiting 5 minutes take and record the measurement on the Blood Pressure Quality Assurance Form.
6. After waiting 1 minute, take a second measurement with the Omron B machine and record the measurement on the Blood Pressure Quality Assurance Form.
7. Remove the Omron B cuff and attach the Omron A cuff to the second volunteer's right arm. Wait 1 minute and then take and record the measurement on the Blood Pressure Quality Assurance Form.
8. Repeat the steps listed for items 1, 2, 3, and 4 above for the third volunteer.
9. Repeat the steps listed for items 5, 6, and 7 above for the fourth volunteer.

10.5.1.2 Blood Pressure Quality Assurance Form Completion:

The Blood Pressure Quality Assurance Form is to be completed monthly on 4 separate persons. The form should be photocopied and e-mailed as a PDF to the Data Coordinating Center by the last day of each month. Field center staff should also complete the form, if they suspect there may be problems with the Omron 705 readings, e.g., readings that seem too high or too low.

The following should be completed on this form:

1. Enter the date of the comparison blood pressure measurements, using year/month/day format, entering the last digit of the year.
2. Enter the HAPO staff ID of the person performing the blood pressure measurements.
3. Enter the serial number of each of the Omron 705 machines.
4. Enter each of the Omron 705 blood pressure measurements (enter the value for Omron A for the first and second measurements and then the value for Omron B) on the first person, as systolic/diastolic, using leading zeroes as necessary.

5. Enter the Omron 705 blood pressure measurements (enter the value for Omron B for the first and second measurements and then the value for Omron A) on the second person as systolic/diastolic, using leading zeroes as necessary.
6. Enter each of the Omron 705 blood pressure measurements (enter the value for Omron A for the first and second measurements and then the value for Omron B) on the third person, as systolic/diastolic, using leading zeroes as necessary.
7. Enter the Omron 705 blood pressure measurements (enter the value for Omron B for the first and second measurements and then the value for Omron A) on the fourth person as systolic/diastolic, using leading zeroes as necessary.
8. Calculate the average of the 4 second and third values for each Omron 705 separately and record them (round to the nearest whole number).
9. Enter the date the form was e-mailed to the Data Coordinating Center, using year/month/day format, entering the last digit for the year. Check the box at the top of the form to indicate it was e-mailed to the DCC.

Compare the systolic and diastolic readings obtained. If the average of the 4 systolic or diastolic readings differs by more than 10 mm Hg, repeat the comparison measurements on an additional 4 persons by completing a second Blood Pressure Quality Assurance Form. If the average of the 4 readings differ by more than 10 mm Hg, contact Lynn Lowe, HAPO Follow-Up Study Project Manager for further instructions.

Note: Whenever a second Blood Pressure Quality Assurance Form is completed, it should be sent via e-mail to the Data Coordinating Center.

Note: The Blood Pressure Quality Assurance Form is not entered into the REDCap Data Entry System.

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BLOOD PRESSURE QUALITY ASSURANCE FORM
OMRON VS OMRON

Note: Use this form to record comparison blood pressure measurements with your two Omrons each month, or whenever there is a concern about one of the Omron electronic machines. Comparison measurements are to be obtained on 4 separate persons, alternating the order of the measurements for the two Omron machines. Once this form has been completed, make a pdf of it and email the form to the Data Coordinating Center. Do not place the form in a HAPO participant folder.

1. Date of duplicate blood pressure measurements: **2 0 1** __ **/** __ __ **/** __ __
Year Mo Day

2. HAPO staff ID of person performing duplicate measurements: __ __ __ __ __ __

3. a. Serial number of Omron 705 electronic machine A: __ __ __ __ __ __ __ __

b. Serial number of Omron 705 electronic machine B: __ __ __ __ __ __ __ __

4. First person:

a. Omron **A** BP: __ __ __ **/** __ __ __ mmHg

b. Omron **A** BP __ __ __ **/** __ __ __ mmHg

c. Omron **B** BP __ __ __ **/** __ __ __ mmHg

5. Second person:

a. Omron **B** BP: __ __ __ **/** __ __ __ mmHg

b. Omron **B** BP __ __ __ **/** __ __ __ mmHg

c. Omron **A** BP __ __ __ **/** __ __ __ mmHg

6. Third person:

a. Omron **A** BP: __ __ __ **/** __ __ __ mmHg

b. Omron **A** BP __ __ __ **/** __ __ __ mmHg

c. Omron **B** BP __ __ __ **/** __ __ __ mmHg

Continued on next page

7.	Fourth person:	**a.** Omron **B** BP __ __ __ **/** __ __ __ mmHg
		b. Omron **B** BP __ __ __ **/** __ __ __ mmHg
		c. Omron **A** BP __ __ __ **/** __ __ __ mmHg
8.	Average of 2nd and 3rd BP measurements (round to nearest whole number)	**a.** Omron **A** BP __ __ __ **/** __ __ __ mmHg
		b. Omron **B** BP __ __ __ **/** __ __ __ mmHg
9.	Date this form was sent to the Data Coordinating Center (DCC):	**2 0 1** _ **/** __ __ **/** __ __ Year Mo Day

NOTE: Make a pdf of this form and email it at the end of each month to the HAPO Data Coordinating Center. Do NOT enter this form into the REDCap Data Entry System.

10.5.2 Anthropometric Measurements

There are many possible sources of error in making anthropometric measurements. These include use of uncalibrated equipment, improper positioning of the subject, incorrect or variable placement of recording devices, and transcription errors. To attempt the highest quality readings for HAPO, the following approaches will be used:

- Central training and certification for master training;
- Use of a "Train the Trainer" approach for research staff unable to attend master training
- Use of duplicate readings;
- Instrument calibration procedures;
- Yearly recertification which includes observation of technique; review of procedures and videos, and duplicate measurements of 3 study subjects which will be obtained by all anthropometric certified study staff (including master trainer)
- Random monitoring of between and within subject) variability, digit preference, etc.

Master training for anthropometric certification requires: 1) participation in central training and observation of performing these measurements, 2) evidence by direct observation at central training that all elements of measurement are followed (placement of tapes, preparation of the participant); 3) evidence of agreement of 3 replicate readings within 1.0 cm for Height, and circumferences; and 1.0 mm for skinfolds 4) evidence of agreement with the standard (HAPO Trainer) with available practice subjects. Research staff who do not attend central training may be trained and certified by the site specific master trainer using the Anthropometric Certification Checklist form.

Equipment should be calibrated and documented each day it used:

- Stadiometer: Daily calibration can be accomplished using a standard (600-800 mm) calibration rod. Calibration checks are performed by measuring the height of the standard rod and recording the measurement obtained. If the standard calibration rod

does not measure correctly, the supervisor in charge of equipment maintenance for the research equipment should be notified and repaired prior to measuring a subject.

- Skinfold Calipers: Daily calibration can be accomplished by using a standard 15mm calibration block. Calibration checks are performed by inserting the block lengthwise into the jaws of the calipers and recording that the calipers are calibrating correctly. If the 15 mm calibration block does not measure correctly, the supervisor in charge of equipment maintenance for the research equipment should be notified.

10.6 Data Forms

The Protocol, Manual of Operations, and data forms have been prepared in English. For field centers with a primary language other than English, or field centers that have > 10-15% participants that prefer conversing in a language other than English and local HAPO Follow-Up Study staff are fluent in that language, local translations of the HAPO Study Summary, HAPO Follow-Up Study Description, HAPO Follow-up Study Identification Form, Screening Form, Recontact Screening Form, exam visit instruction sets, Test Qualification Forms for both Mother and Child, Questionnaire, forms related to use of Metformin in mother and child, and Future Contact Information Form are to be made and sent to Chicago for approval. Back-translation of these forms and documents will be made without reference to the original. Comparison will then be made with the original English version, and discrepancies referred back to the field center for clarification. To minimize errors in data entry, it is particularly important that translated versions of the data collection forms maintain the structure of the English originals, and efforts need to be made to ensure that questions line up correctly with answer boxes on the right-hand side of the forms. Data forms that are not administered to participants will not be translated. To maintain standardization of forms, it will not be permissible for field centers to use an interpreter to translate forms for use with participants who do not converse in the language(s) of the forms.

Field centers must print or photocopy the data collection forms for routine use during data collection. Each data collection form page contains space for a participant ID label. Pages of labels for each ID number are supplied centrally by the Data Coordinating Center to each field center. If possible, form sets for each ID number with labels attached should be prepared in advance for use as women are recruited and enrolled in the follow-up study. Prepared form sets should be stored in the polypropylene file folders provided by the Data Coordinating Center. Labels for the blood sample tubes and cryovials should also be stored in the folder.

10.7 Standardized Equipment and Supplies

To standardize methods of data collection and entry and ensure standardized handling of blood specimens, each field center must have the following equipment: 1) centrifuge, preferably refrigerated; 2) -20^{0}C or colder freezer for storage of blood samples, with back-up power or an alarm system for notification of freezer failure, and a backup procedure for maintaining specimens in the frozen state; 3) a desktop or notebook computer with high-speed Internet access for data entry of completed forms into the HAPO Follow-Up Study REDCap data base; and 4) access to a photocopier, preferably a multi-function copier/scanner capable of converting documents to PDF files that can then be e-mailed to the Data Coordinating Center.

The Clinical Coordinating Center will provide phlebotomy supplies to each field center, the glucose doses for the OGTT, the BOD POD, as well as supplies for the BOD POD, including bathing caps and swim suits. Each field center will also be provided with storage vials and freezer boxes for blood and urine specimens, and with polyurethane boxes for shipment of blood and urine specimens. Each field center must have local access to dry ice and air freight delivery to the Laboratory Coordinating Center that can be guaranteed within 48-72 hours.

The Data Coordinating Center will provide the following to each center: 1) Manual of Operations, Protocol, data forms, Recruiting Register for determining the order of recruitment of follow-up study participants, Call Back Register to list women or children that need to be called back in regards to medications (including use of metformin), or missed study visit; 2) training materials; 3) pre-printed labels for data collection forms; 4) pre-printed labels for blood sample tubes, urine specimen cups, cryovials, and freezer boxes; and 5) file folders for data collection forms and labels.

10.8 Data Editing

To improve the quality of data collection and minimize the need for corrections before and after data entry, the following principles need to be adhered to in completion of all forms:

- Write legibly in ink. The data entry person will not be able to enter data that are illegible, or may enter illegible data incorrectly. It is preferable to use some other ink color than

black to make it easier for the data entry person to read (e.g., blue). Red ink should only be used for making corrections.

- Do not leave any data fields blank, unless the form instructs you to do so, *or if a numerical value is unknown.*
- Enter dates correctly, using year/month/day format.
- Transcribe data carefully to minimize transcription errors.
- Review each completed form prior to data entry for illegible entries, missing or blank entries, marks between boxes or multiple boxes checked, incorrect or impossible dates, etc.
- Clearly identify corrections.

Correct all data forms as follows:

- Make each correction in red ink.
- Draw a single line through the incorrect response leaving the original entry readable (do NOT use "white-out").
- Write the correct response near the incorrect response or check the correct box.
- Circle the correct response and put your initials and the date near the circle.

If a form contains illegible entries, missing data, multiple boxes checked when only one is to be checked, or checks between boxes, seek clarification of the items in question from the staff member who completed the form. If the staff member is unable to resolve the problem and the participant would not be able to provide the correct data, circle the answers in red ink and write the letters NR beside the answers for "Not Resolvable", and initial it. This will instruct the data entry person to enter the appropriate "missing value" code during data entry. If the form was an interviewer-administered questionnaire, and the participant has left the clinic, attempt to obtain the data as soon as possible. Set the form aside until the correct data are obtained and entered on the form. If, for some reason, the correct data cannot be obtained, circle the answers with red ink, write the letters NR beside the answers, and initial it.

10.9 Documentation of Recruitment

It is essential that accurate records be kept of participant recruitment for the follow-up study, including information on refusals and exclusions, and that study IDs be correctly utilized, i.e. that participants be given the same ID they were given in the original HAPO Study. A Recruiting

Register listing eligible HAPO Study participant IDs will be prepared centrally for day-to-day use in each field center. The DCC will preprint the Recruiting Register with the HAPO IDs of women who are to be invited to participate. The ordering of the IDs will be based on the birth date of the child, in order to ensure that mothers with the oldest children are contacted first. All women known to meet inclusion criteria for the follow-up study will be included. In order to ensure that names are correctly matched with HAPO IDs, the Data Coordinating Center will also preprint the birth dates of both the mother and child, based on the original HAPO data set, so that field center staff can verify that they are contacting the correct person. Use of the Recruiting Register is described in **Chapter 3. Recruitment.** Data on recruitment will be used to help the Data Coordinating Center monitor follow-up study participation rates for each field center over the course of field work and at the end of field work allow comparison of original HAPO Study data between participants and non-participants in each field center, as well as comparison of participation rates across centers.

10.10 Data Entry

Data entry will be done at each field center, using REDCap, a secure web-based software package for data entry and management, developed for use as part of the CTSA – Clinical & Translational Science Awards. Field center staff will enter completed forms through a high speed Internet connection. *Data are to be entered into REDCap within 2 working/business days of a study visit.* During data entry, data will be subject to range and logic checks. Procedures for accessing and using REDCap are described in **Chapter 9**. Instruction on data entry procedures will be included at Central Training. Entered data will be imported from REDCap by the Data Coordinating Center weekly as SAS data sets. All data forms containing key data will be double-entered. Discrepancies in double entry will be communicated automatically by REDCap to the individual entering the data and any errors should be resolved immediately.

After a form has been entered into the HAPO Follow-Up Study REDCap data base, the data entry person should enter his or her staff ID in the spaces marked: “HAPO staff ID of person entering data into Data Entry System” at the end of the form. In addition, an “X” should be placed in the box at the top of the first page of the form marked “Data Entry Done” to indicate that the data on the form have been entered.

10.11 Processing Field Center Data at the Data Coordinating Center

As soon as possible after receipt of field center data at the Data Coordinating Center, an initial computer check will be carried out to confirm that no systematic errors are being made in data collection. Checking programs will also test whether the data are internally consistent. A list of unknown or missing fields will also be produced. Every effort will be made to ensure that imported data have this checking procedure carried out within 48-72 hours. If major problems are identified, the field center will be contacted by telephone, FAX, or e-mail. In urgent cases, where the Manual of Operations appears not to have been followed or has been misunderstood, Data Coordinating Center staff will contact the field center PI and/or Research Nurse/Coordinator by telephone and e-mail, with the e-mail providing documentation of the problem. A log of all such communications will be maintained for periodic review by senior Coordinating Center staff.

10.11.1 Communication of Errors to Field Centers

Field center errors will be detected at various stages of the review procedure. In general, errors will be of two types:

- Major (systematic) errors: These arise from misinterpretation of the Protocol or Manual of Operations, and result in incorrect recording of data. They will be discovered at the Dry Run or during the computer checks. In all cases, contact with the field center is to be made immediately by telephone and e-mail, so that corrective action can be taken.
- Minor errors: These occur when information is missing, incorrectly entered, out of range, etc. They will generally be found during data entry or by the data checking programs at the Data Coordinating Center. Errors discovered by the checking programs at the Data Coordinating Center will be reported to the field center by e-mail using a Problem Report by form and participant ID for review and correction by field center staff. Pages of these Problem Reports are to be filed in a loose leaf binder following local entry of the correct values into the REDCap data base. However, for these reports a copy is also to be forwarded to the DCC by e-mail as a PDF at the Data Coordinating Center. A computer transaction file of errors, omissions, inconsistencies, or other problems will be maintained. The transaction file will be updated whenever an error report with corrections is received from the field center. Summary reports will also be prepared for

review by senior staff on the number of requests made for corrections by the data checking programs, the number satisfactorily resolved, the number still outstanding, etc.

10.11.2 Correction of Errors

Field center staff will enter corrections *for issues noted in Problem Reports* locally into the REDCap data base. These reports contain the form name or names, participant ID, question numbers, the value or values entered, and space for writing in the correct values. Only the correct values are entered into the data system. Copies of completed Problem Reports for errors found during data checking at the Data Coordinating Center will be *returned* by e-mail by the field center within 2 weeks of receipt.

10.12 Communications

The Coordinating Centers will maintain close contact with each field center throughout the study. This will take the form of regular general communications (e.g., updates to the Manual of Operations, Newsletters, etc.) and direct contact at different stages of the study locally. Separate files and a "field center notebook" will be kept to record details of communications with each center.

Lines of communication will be established in advance of data collection, so that field errors can be detected and corrected as quickly as possible. In all cases, Coordinating Center staff are to be on hand to answer queries arising in the field. Urgent problems will be dealt with by telephone, FAX, or e-mail. Other queries will also be handled by e-mail and a standard form for this purpose will be prepared. Chicago will also advise each field center on whether shipments of blood and urine specimens have been received.

After completion of data collection, a request will be made for specimen shipping lists, as well as answers to any outstanding queries. Once all data have been merged into the database in Chicago, checked and verified, a summary report of data received will be prepared and sent to the field center PI.

10.13 Retraining

The Steering Committee, Clinical Coordinating Center, and Data Coordinating Center will develop criteria that will be used to determine whether a staff member(s) in a particular field center needs to be retrained. For field centers in which two persons have been trained, e.g., a PI and a Research Nurse/Coordinator, or two Research Nurses, duplicate measurements (child skinfolds, waist circumference, mid-arm circumference and mother waist and hip circumference) may be made by these two persons on 5% or 10% of participants, with the request that measurements be completed independently by each person. Criteria for retraining will also involve the number of missing data items for questionnaires.

On an ongoing basis, mean values for continuous measurements will also be compared by staff member within and between centers, e.g., child anthropometric measurements, maternal height and weight, maternal and child blood pressure, etc. Values will also be monitored over time for each staff member within a center, by comparing monthly means for that person, to assess consistency of measurement over time. While differences within and between centers, and within the same staff member, may be real, criteria will nonetheless be developed for identifying potential problems. Steps that will be taken to deal with problems identified during this process include decertification of a staff member for particular areas of data collection, if there is a second staff member available who is also trained in those areas; or suspension of recruitment, pending retraining, either at the local center, through a site visit from Coordinating Center staff, or through travel by the staff member to the Coordinating Center.

10.14 Laboratory Coordinating Center

Regular meetings among the staff of the three Coordinating Centers will be held to review laboratory and quality control procedures, including backup of laboratory data. Other items of interest will also be discussed, including transfer of data, shipping, and finances. Plots of internal quality control samples will be periodically shared with the Executive Committee for review.

A close working relationship will be established among the three Coordinating Centers with detailed minutes kept of all meetings.

10.14.1 Notification of Biological Sample Shipments

Both the Clinical and Laboratory Coordinating Centers are to be advised of incoming shipments from field centers. Once the shipment has been received and the boxes opened, an inventory of aliquots is to be taken and compared with the storage box shipping list from the field center, and an assessment made of the state of the samples (whether thawed, whether tubes are cracked, whether labels are intact, etc.) with appropriate feedback to the field center given. Forms documenting the date of arrival of each shipment, the IDs of samples received and the state of the samples are to be kept. In the exceptional case, where shipments have thawed or gone astray, alternative routes of shipping will be reviewed with the field center PI.

The shipment containing the first set of blood samples from each field center is to be analyzed quickly by the Laboratory Coordinating Center and a report prepared identifying any problems in labeling or in use of IDs. If necessary, the field center will be contacted urgently for a review of local procedures.

10.14.2 Quality Control Procedures

An extensive system of internal quality control for the HAPO Follow-Up Study will be developed by the Laboratory Coordinating Center in collaboration with the Clinical and Data Coordinating Centers. Regular review of the quality control procedures will be carried out during meetings with Laboratory Coordinating Center staff.

- Participant IDs: Aliquot tubes will be sent to the Laboratory Coordinating Center with Bar-code labels containing the original HAPO participant ID and aliquot code. These labels will be read at the Laboratory Coordinating Center using a Bar-code reader for direct entry into the computer of the ID and sample result. Use of Bar-code labels minimizes any problems that could arise from transcription of aliquot IDs or sample results onto laboratory working sheets. The computer list will be forwarded to the Data Coordinating Center for comparison against the Shipping List to ensure that the labels have been read correctly and that all specimens listed were in fact sent. Any discrepancies will be investigated, and if necessary checked with the field center. Confirmation of the full 8-character aliquot ID will allow the laboratory data to be merged with the mother's or child's other data at the Data Coordinating Center, and allow the Data Coordinating Center to identify the specific measurement, e.g. a child's fasting glucose value.

- Duplicate samples: In the original HAPO Study, a random 5% of IDs were chosen in advance for this purpose. In order to simplify procedures for the follow-up study, we will randomly select 5% of participants to have their backup samples analyzed. Results for 'Analysis' and 'Backup' samples will be reviewed and any gross discrepancies checked first for mislabeling in the laboratory and then for mislabeling in the field. A formal analysis of laboratory technical error will be undertaken once computerized laboratory data are received at the Data Coordinating Center.

10.15 Processing Laboratory Coordinating Center Data

At the Laboratory Coordinating Center, computer entry of aliquot IDs and sample results will be automated through use of Bar-code labels containing the participant ID and aliquot code on all tubes and cryovials shipped to the Laboratory Coordinating Center. When laboratory data are transferred to the Data Coordinating Center, they will be processed through checking programs for range and consistency checks and then merged with the corresponding participant data in SAS data files, using the first 5 characters of the participant ID and 3-digit aliquot code as identifier. An automated record keeping system will be developed that will produce a monthly summary of the number of sample results received, and the number of participants for whom laboratory data have been received and merged into the data base.

For day-to-day running of the study, additional data will also be received from the Laboratory Coordinating Center:

- Results on first sample shipment: Blood samples from the first shipment from each field center will be analyzed very soon after receipt at the Laboratory Coordinating Center. Duplicate samples in this shipment are to be identified, and if gross discrepancies are apparent, the samples re-analyzed to determine whether mislabeling of the specimens has occurred, either in the field or in the Laboratory Coordinating Center.
- Inventory of blood and urine samples: Lists of blood and urine samples received with date of arrival, state of arrival, etc., are to be stored on computer and transferred to the Data Coordinating Center as shipments arrive. Comparison of IDs is to be made with those in data transmissions, and any discrepancies investigated.

10.16 Quality Control Reports

The Data Coordinating Center will prepare reports on an ongoing basis on study progress, and on the performance of the Laboratory Coordinating Center. Reports specifically requested by the OSMB will also be prepared.

10.16.1 Reports on Study Progress

Reports on study progress will include monthly tabulations by field center of the number of women enrolled and current rate of recruitment compared with that required to achieve each center's recruitment goal; number of women and children completing data collection; number of forms downloaded from the HAPO Follow-Up Study REDCap data base, number processed since last report, number that generated edit messages, current edit message rate per form, number of forms with missing data, and number of unanswered edit queries.

The Data Coordinating Center will also on an ongoing basis compare mean values for continuous measurements by HAPO field center staff member within and between centers, e.g., child and maternal anthropometric measurements, maternal and child blood pressure, etc. The Data Coordinating Center will also monitor mean values over time for each HAPO field center staff member, by comparing monthly means for that person, to assess consistency over time.

10.16.2 Reports on Laboratory Performance

Reports on laboratory performance will include monthly tabulations of the number of samples received at the Laboratory Coordinating Center; the number thawed, lost, or unusable; number of samples requiring reanalysis, including reasons for reanalysis; backlog of samples remaining to be analyzed; summary of any events affecting laboratory operation, e.g., power outages; review of internal and external quality control reports; and calculation of mean differences, correlations, and technical errors from submission of 'Backup' samples. The Data Coordinating Center will also tabulate the number of women with data transferred from the Laboratory Coordinating Center to the Data Coordinating Center.