SECTION 10. QUALITY CONTROL OF STUDY DATA

10.1 Introduction

In addition to the quality control methods and programs routinely used at clinical center laboratories and central laboratories, quality control mechanisms for the AASK Study are outlined in the following sections.

10.2 Local Biochemistry Laboratories

Intentionally left blank.

10.3 GFR Procedure

For quality control of the clinical center GFR procedure:

1)The coefficient of variation (CV) of the GFR for each GFR collection period and the urine flow rates of each GFR measurement are reported to the clinical centers, and these CVs are summarized and analyzed by the Data Coordinating Center and reported to the Data Monitoring Subcommittee.

2)A staff member of the Central GFR Laboratory who is familiar with the AASK protocol will participate in site visits of the clinical centers. The representative of the GFR Lab will arrive one day prior to the rest of the site visit team to observe the GFR technician conducting a GFR, answer questions, and offer suggestions if a problem (i.e., results from a center are erratic or inconsistent) with a center's GFR measurements or procedures is identified.

10.4 Blood Pressure Measurements

Quality control is maintained by centralized training of at least one technician from each clinical center, by certification of all technicians performing blood pressure measurements, by quarterly calibrations of RZ machine with results recorded in a log maintained at the clinical center, weekly inspections of the RZ device, and by duplicate measurements taken on a periodic basis on quality control individuals (study or non-study individuals). Throughout the study period, the technician performs all blood pressure measurements on quality control individuals concurrently with a second technician performing these measurements on the same individual.

The Quality Control Subcommittee reviews diastolic and systolic blood pressure values for digit preference and differences in duplicate measurements and means by the center and the technician. The subcommittee reviews the use of non-certified technicians for blood pressure measurements and for any other deviations from protocol. Those individuals having digit preference on two consecutive reports must retake and

successfully complete the videotape test.

10.5 Site Visits

Site visits are to be made to each of the Clinical Centers during years 1 and 2. The primary goals of the site visits are: 1) to observe the clinic under normal operating conditions for adherence to protocol; 2) to increase/improve communication between the study administration, the clinic personnel and the DCC; and 3) to demonstrate the trial's concern for the quality of data collection. Site visit teams consist of a site visit chair from the Quality Control Subcommittee, a DCC staff member familiar with the AASK protocol and the blood pressure requirements, a NIH representative, a member of the GFR lab staff and a Study Coordinator from another clinical center. Pre site visit reports will be compiled by the DCC. All site visit teams will compile a post site visit report which is given to the Clinical Center PI and to the NIH. These reports are reviewed by the Quality Control Subcommittee.

A special committee will be formed to site visit the DCC. The exact membership of this committee will be determined by NIDDK. It is expected to include a representative from NIDDK, representatives from one or more of the Clinical Centers, a representative from the External Advisory Committee, a biostatistician and a database expert. Ideally both the biostatistician and the database expert will have clinical trials expertise. The Chairman of the Steering and Planning Committee may be included.

10.6 Quality Control of the Central Biochemistry Laboratory

Data from the Central Biochemistry Laboratory will be handled in the same manner as Clinical Center data; i.e., data will be entered and verified in the database on the Cleveland Clinic Foundation SUN with a subset later selected for additional quality control. Appropriate edit checks will be in place at the key entry (database) level.

The Central Biochemistry Laboratory has an internal quality control system established. This system is outlined in the Manual of Operations for the Central Biochemistry Laboratory.

This system includes:

1)The inclusion of at least two known quality control samples; the reported measurements of the quality control samples must fall within specified ranges in order to be certified as acceptable.

2) Calibration at FDA approved manufacturers' recommended schedules.

External Quality Control of the Central Biochemistry Lab: Every six months, the Data Coordinating Center will notify each Clinical Center to perform external QC for one serum and one urine specimen. External CBL QC will be restricted to annual visits at which the complete set of serum and urine analyses are conducted. The Data Coordinating Center will provide the QC ID number (QC IDs will contain 6 digits, the first two digits designating the Clinical Center, and the third digit equal to 9). Each Clinical Center should use the Namecode specified in question 6 when completing Form 61. A first choice and two alternating choices as to which patients' serum and urine specimens to QC will be provided. In most cases, the serum and urine QC will be done on different patients. The center should use the first choice listed on the printout provided by the Data Coordinating Center. The second choice can be used if the patient listed as the first choice misses the scheduled visit. The procedures at the Clinical Center are as follows:

Amount required for Serum: Draw three 10 ml SST vacutainer tubes, or other type tubes which have no anti-coagulant in them. The minimum amount of serum needed is 4 mls.

Sample Processing of Serum and Urine:

1)Label one set of mailing types with the QC ID and Namecode. Label a duplicate set of tubes with the patient information.
   a.Split the urine sample by mixing the entire 24-hour collection well and aliquoting two tubes with approximately 25 mls in each.
   b.Split the serum sample by spinning all SST vacutainer tubes. Pour off the serum from these tubes into one container. Mix well and pour at least 4 mls into the "QC" tube and at least 8 mls into the patient tube.
   c.Put tubes in a ziplock bag.

2)Do not send the serum or urine "QC" sample and the real sample in the same shipment. Send the QC sample within the next day or two of sending the "Real Sample."

3)A Serum or Urine Mailing Form (Form 22 or 23) does get filled out but does not get key entered for each serum or urine QC sample that is sent.

4)The Clinical Center should enter and verify Form 61 for the QC sample being sent to the CBL. **However, do not send Form 61 with the QC sample to the CBL.

5)The CBL will receive the QC sample and will handle them in the same manner as a patient sample. Form 18 and 19 are filled out as for a regular patient.

10.7 Quality Control of the Central GFR Laboratory

Data from the Central GFR Laboratory will be entered and verified by the Central GFR Laboratory staff. Appropriate data integrity checks will be in place in the DCC study database.

The Central GFR Laboratory has an internal quality control system established prior to analyzing any AASK samples. This system is outlined in the Manual of Operations for the Central GFR Laboratory.

This system includes:

1)The pipette used for GFR samples is routinely evaluated for volumetric accuracy and precision using the weighing of water on an electronic microbalance as a quality control technique.

2)The gamma counter is calibrated with ^{137}cesium standards to ensure accurate peak locations and window settings.

3)The counter efficiency is monitored daily using ^{137}cesium standards. Counter background activity is monitored on a daily basis as well.

4)The participant counts are bracketed by matched ^{125}I-sodium iothalamate standards to eliminate instrumental malfunctions during sample counting as an error source.

5)A reproducibility study is performed weekly by selecting a GFR study and remeasuring the specimens the following day.

External Quality Control of the Central GFR Lab: Whenever a clinical center sends GFR specimens to the Central GFR Laboratory, back-up specimens should be saved. Every six months the Data Coordinating Center will notify each Clinical Center to

perform external QC for one GFR specimen. External GFR QC will be restricted to annual visits. The Data Coordinating Center will provide the QC ID number (QC IDs will contain 6 digits, the first two digits designating the Clinical center, and the third digit equal to 9). Each Clinical Center should use the Namecode specified in question 6 when completing Form 61. A first choice and two alternative choices as to which patients' GFR specimen to QC will be provided. The center should use the first choice listed on the printout provided by the Data Coordinating Center. The second choice can be used if the patient listed as the first choice misses the scheduled visit.

Sample Processing of GFR:

1)After the GFR results come back from the Central Laboratory, the Clinical Center technician will prepare a patient's back-up specimen for mailing, using the appropriate QC ID number and the center's QC Namecode (listed on Form 61, question 6) on the tubes and on the mailing form.

2)A GFR Mailing Form (Form 24) does get filled out but <u>does</u> <u>not</u> get key entered for each GFR QC sample that is sent.

3)The Clinical Center should enter and verify Form 61 for the QC sample being sent to the GFR Lab. **However, <u>do</u> <u>not</u> send Form 61 with the QC sample to the GFR Lab.

4)The GFR Lab will receive the QC sample and will handle them in the same manner as a patient sample. Form 25 is filled out as for a regular patients.

Results of the first GFR and the second GFR will be compared for quality control.