SECTION 14. FOLLOW-UP PERIOD (VISITS FV-1...FV-N)

14.1 Routine Follow-up Visits

The follow-up period will last up to 84 months, depending on the date that the participant is enrolled and randomized. The study coordinator must keep close track of participant visits during this period as different measurements and activities occur at different visits. Visits will be according to the schedule in Table 18.2 of the Protocol and will occur within ±15 days of the scheduled visit date during monthly visits in the first 6 months, and ± 30 days for the subsequent visits every two months, otherwise a Missed Visit Form (#11) should be completed. The target date for the FV1-0 visit is one month from G2. There is no minimum window but the maximum window is 45 days.

14.1.1 Clinical Assessment

During the follow-up period participants will be seen according to the protocol schedule in order to achieve or maintain blood pressure control and to obtain safety and study-related data. At routine FVs, if there is any change in reported symptoms, the participant will undergo a limited history and physical examination including vital signs and weight, compliance assessment, and assessment of adverse drug reactions or intercurrent illness.

14.1.2 Blood Tests

Blood will be collected according to the schedule in Protocol Table 18.1 and 18.2.

9.5 ml Serum separator tube for SMA 18
9.5 ml Serum separator tube for fasting lipid profile
7 ml Plasma (EDTA) tube for CBC

Blood will be processed for mailing to the Central Laboratory (SMA 18 and Lipids) and Form #22 completed. The CBC is done locally (Form # 13).

During Follow-Up, if a sample which is collected according to the "Completion Schedule" and is received at the Central Biochemistry Laboratory and is found to be hemolyzed, the sample may not be re-drawn. In this case, the Central Biochemistry Laboratory will analyze what they can, and the remaining values will be missing. However, if a serum sample is collected due to an Action Item or at the FV0-1 Safety Visit and is received at the Central Biochemistry Laboratory and is found to be hemolyzed, the serum should be recollected.

During Follow-Up, if a serum and urine sample are collected at a visit where a GFR is required according to the "Completion Schedule", but for some reason the GFR is aborted, the serum and urine specimens should be sent to the Central Lab for processing. If the patient returns within the same visit window in order to obtain the GFR, the serum

and urine should be recollected. If the GFR is successful and the CBL measures the blood and urine successfully, the clinical center should send an inquiry to the DCC asking to delete the serum and urine mailing forms and results for the first sample collected in which the GFR was aborted so that the serum and urine mailing forms and results can be entered for the visit where the GFR was successfully performed. This will facilitate collecting complete creatinine clearance data.

14.1.3 GFR Measurements

In addition to the above procedures, GFR will be measured at FV-3, FV-6, and every 6 months thereafter. A serum pregnancy test will be performed locally before GFR visit and the result recorded on the GFR Form #24. Participants with a positive test will not undergo the GFR. If the test is negative the GFR will proceed as described previously. During Follow-Up, if a CV for a GFR is >50%, the GFR does not need to be repeated.

During Follow-Up, if a serum and urine sample are collected at a visit where a GFR is required according to the "Completion Schedule", but for some reason the GFR is aborted, the serum and urine specimens should be sent to the Central Lab for processing. If the patient returns within the same visit window in order to obtain the GFR, the serum and urine should be recollected. If the GFR is successful and the CBL measures the blood and urine successfully, the clinical center should send an inquiry to the DCC asking to delete the serum and urine mailing forms and results for the first sample collected in which the GFR was aborted so that the serum and urine mailing forms and results can be entered for the visit where the GFR was successfully performed. This will facilitate collecting complete creatinine clearance data.

14.1.4 Urine Tests

The participant will bring a 24-hour urine sample for measurement of sodium, potassium, creatinine, urea and protein at B1, FV6 and every six months thereafter. Twenty-four hour urine samples will be collected in containers, with 250 cc 5% acetic acid added as a preservative for urea, provided to the participant on the preceding visit. A 20 ml aliquot of each urine will be mailed to the Central Biochemistry Laboratory in a labeled container along with Form #23. A duplicate 25 cc urine aliquot will be frozen at -20 and stored locally.

During Follow-Up, if a serum and urine sample are collected at a visit where a GFR is required according to the "Completion Schedule", but for some reason the GFR is aborted, the serum and urine specimens should be sent to the Central Lab for processing. If the patient returns within the same visit window in order to obtain the GFR, the serum and urine should be recollected. If the GFR is successful and the CBL measures the blood and urine successfully, the clinical center should send an inquiry to the DCC asking to delete the serum and urine mailing forms and results for the first sample collected in which the GFR was aborted so that the serum and urine mailing forms and

results can be entered for the visit where the GFR was successfully performed. This will facilitate collecting complete creatinine clearance data.

The database will accept 24-hour urine collections that are completed outside of the appropriate Protocol visit window (as specified by the "Forms Completion Schedule").

Centers should do everything possible so that the 24-hour urine is collected within the appropriate Protocol visit window. However, if the 24-hour urine cannot be collected within the appropriate window, centers can now collect the urine and enter this information (Form 23) if the 24-hour urine is collected outside of the window. Form 23 should be labelled with the visit window that the urine was actually collected in.

The reported creatinine clearance will be calculated by finding the closest serum that was collected since the database still does not accept serums that are collected outside of the visit window.

14.1.5 Interventions

Appropriate instructions regarding lifestyle modifications will be administered to the participant as outlined previously. Blood pressure medication(s) adjustments will be performed as described in the intervention section.

14.1.6 Blood Pressure Measurement Procedures

All blood pressure measurements conducted by AASK Study Personnel on AASK patients must be recorded in the data base, regardless of the clinical condition of the patient at the time of the measurement. This includes blood pressure measurements taken on days of GFR visits, and at both protocol and interim visits.

If more than one RZ blood pressure measurement is obtained on the same patient the same day, then:

1) Form 10s must be completed for each RZ blood pressure measurement that is taken

2) The Form 10 for the FIRST RZ blood pressure must be keyed by the center into the AASK data base

3) Form 10s for all additional RZ blood pressure measurements recorded on the same day should be faxed to the DCC

4) The complete AASK protocol for blood pressure measurements must be followed for each measurement

All blood pressure measurements taken by AASK personnel should be done by the random zero sphygmomanometer if at all possible. If blood pressure measurements are taken by AASK personnel on AASK patients using non-RZ devices at any time, these measurements must now be recorded on the Form 9 Non-RZ blood pressure form.

Blood pressure measurements conducted by AASK study personnel on AASK patients should be conducted at the AASK clinic or a satellite office if at all possible. This applies both to protocol and interim visits.

Details:

A. In exceptional circumstances blood pressure measurements may be conducted outside the AASK clinic or satellite office (e.g. at the patient's home or work), but the frequency of such measurements should be kept as small as possible.

B. A new item on Form 11 will now capture the location of all visits, so that for some analyses in-home blood pressure measurements can be assessed separately from measurement conducted in the AASK clinics.

14.2 Non-Protocol Visits

Non-protocol visits may be scheduled as frequently as necessary between the scheduled visits during the Follow-up Period. Interim visits may be scheduled to ensure that the participants assigned MAP goal is achieved or maintained by adjustment of antihypertensive medication; that compliance with the protocol is achieved; that possible adverse events or symptoms related to adherence to the drug regimen are evaluated; that laboratory tests are measured and evaluated; and that any causes of acute or subacute renal failure are evaluated and, if possible, corrected.

At the end of the FV0-0 visit, all randomized participants will be scheduled to return to the clinic in 5-7 days for Visit FV0-1. A serum creatinine, potassium and CBC will be measured to detect any acute deviations in these laboratories. At each interim visit, not simply being held for obtaining laboratory tests, the evaluation will include an interval history, weight and BP (Forms 10 and 11), as well as a limited physical if there has been a change in reported symptoms. The reasons for the interim visits, the findings at these visits, and the actions taken will be recorded on Visit Form #11.