SECTION 1. RECRUITMENT

1.1 Background

Improving the health of African Americans is a major national priority. Evidence of this commitment includes the institutions of large-scale clinical studies specifically focused in diseases which result in a disproportionate burden of illness in the African-American community. The successful conduct of these studies depends on recruitment of an appropriate number of African-American participants to meet the scientific goals of each investigation. Each of the clinical centers collaborating in AASK will utilize different recruitment strategies to assess the effectiveness of each in the recruitment of African Americans for research studies.

1.2 Recruitment Strategies

Each of the clinical centers collaborating in AASK plan to do patient chart reviews as the primary strategy for recruitment.

The specific recruitment approaches employed by the center includes mass mailings to age-eligible African Americans in the community, identified by motor vehicle and voter registration list; as well as community oriented primary care clinics; community screening at shopping centers, fairs, church groups, neighborhood health centers, and work sites; advertisement through the media including radio, television, newspapers and magazines; relatives and friends of dialysis and transplant patients will be approached and referrals from professional groups including pharmacist, black physician, ministers, community advisory groups, black fraternities and sororities and NAACP leaders.

Recruitment materials, including a brochure, have been developed by the Recruitment/ Compliance Subcommittee. These materials can be modified by each clinical center to fit its specific needs and incorporated into its recruitment approach. They can also be used to prepare the community for the beginning of AASK. The recruitment coordinators at each clinical center will keep the coordinating center apprised of specific recruitment methods being employed there and forward copies of recruitment materials to the coordinating center.

1.3 Participant Selection/Eligibility and Exclusion Criteria

1.3.1 Inclusion Criteria

1. African-American men and women (including Black individuals born in the Caribbean, Africa, Canada, etc.) age 18-70 years. Each center should attempt to include both men and women, at least 1/3 of each.

2. Hypertension is defined as a sitting diastolic blood pressure of 95 mmHg or more. Hypertensive participants on antihypertensive therapy need only one

qualifying clinic visit. Those off medication must qualify on two consecutive clinic visits. The average of the last two of three consecutive readings at a single visit is the level used.

3. Reduced renal function, defined as a pre-randomization ^{125}I-iothalamate glomerular filtration rate between 20-65 ml/min/1.73 m^2.

4. Willingness and ability to cooperate with the protocol.

1.3.2 Exclusion Criteria

1. History of malignant or accelerated hypertension within 6 months prior to study entry; previous chronic peritoneal or hemodialysis or renal transplantation.

2. Known secondary causes of hypertension.

3. Any known history of diabetes mellitus type I and II or fasting (8-12 hours) glucose >140 mg/dl on two occasions or random glucose >200 mg/dl on one occasion.

4. A ratio of urinary protein (mg/dl) to creatinine (mg/dl) exceeding 2.5 in a 24-hour urine sample collected at or shortly before the initial GFR visit. (This ratio is used as an estimate of >2.5 g/d proteinuria without needing to factor for validity of the collection.)

5. Clinical or renal biopsy evidence of any renal disease other than hypertensive nephrosclerosis. Persons with arteriographically documented renal arterial atherosclerotic disease less than 50% stenosis of the renal artery should be considered eligible for study participation if the PI at the center feels the disease is not clinically significant.

6. History of drug abuse in the past 2 years, including narcotics, cocaine or alcohol (>21 drinks per week).

7. Serious systemic disease that might influence survival or the course of renal disease. (Chronic oral steroid therapy is an exclusion, but steroid-containing nasal sprays are not. Inactive sarcoidosis is not an exclusion.)

8. Clinical evidence of lead intoxication.

9. Arm circumference > 52 cm, which precludes measuring blood pressure with the "thigh" blood pressure cuff.

Arm length such that if the cuff that is appropriate for the arm circumference extends into the antecubital space so that the cuff would interfere

with placement of the stethoscope over the brachial artery for blood pressure measurement.

10. Clinical evidence of congestive heart failure, current or within the preceding six months. Ejection fraction below 35% measured by any method. Heart block greater than first degree or any other arrhythmia that would contraindicate the use of any of the randomized drugs.

11. Reactive airway disease, current or in the preceding six months requiring prescribed treatment for more than two weeks.

12. Impairments or difficulty in voiding, precluding adequate urine collections.

13. Intake of nonsteroidal anti-inflammatory agents (NSAIDs) more than 15 days/ months, excluding aspirin. Inability to discontinue NSAIDs or aspirin for 5 days prior to GFR measurement.

14. History of serious adverse reaction to any of the randomized drugs required for use in the protocol or contraindication of their use.

15. Pregnancy or likelihood of becoming pregnant during the study period; lactation.

16. Serum potassium level > 5.5 mEq/L,at the SV2 and confirmed at G1 for those <u>not</u> on ACE inhibitors during Baseline, or serum potassium level >5.9 mEq/L at the SV2 and confirmed at G1 for those on ACE inhibitors during Baseline.

17. Leukopenia < 2,500/mm^3 at SV2 and confirmed at the end of Baseline.

18. Medically-indicated need for any of the randomized drugs for any other reason (including angina pectoris, migraine, arrhythmia).

19. Allergy to Iodine.

20. Suspicion that the participant will not be able to adhere to medication or comply with the protocol visit schedule.

21. Participation in another intervention study.

1.4 Pre-Screening Procedure

There are two pre-screen forms which well be used during recruitment. The majority of potential study participants will be identified by chart screening at each of the clinical center chart.

1.4.1 Chart Prescreening Form #01

This form is to be completed on participants considered for entry into the study meeting the following requirements: African-American with hypertension, ages 18-70 years. If the participant is identified through laboratory screening of serum creatinine levels between 1.2 and 4.5 mg/dl for females and between 1.4 and 5 mg/dl for males.

1.4.2. Personal Contact Prescreening Form #02

This form can be self-administered and administered by interview over the phone. The form must be completed all study candidates.

1.5 Completion of Pre-Screening Forms

It is extremely important that in both completing each form and editing it subsequently, the clinic staff is responsible for checking every item to ensure that it has been properly completed and that the information provided is internally consistent. For example, if a YES response to a particular item requires the completion of additional questions asking for more details, clinic staff should note that those questions have been answered. Similarly, if the initial question was answered NO, those additional items should not be completed, and if they have been, it is necessary to clarify the correct response with the participant.

1.6 Informed Consent

1.6.1 General Principles.

In order to be eligible for the study, each participant must be willing to sign a statement of informed consent prior to the Baseline Period, and a statement of informed consent for randomization. This will document the agreement of the participant to participate in the study activities.

1.6.2 Participation in Other Studies.

Participation in the AASK Study is expected to be time consuming. Participants will be asked by AASK Study personnel to not participate in any other research studies during their participation in the AASK Study unless it is an AASK ancillary study reviewed by the Publication, Ancillary Studies and Recruitment Subcommittees and approved by the Steering Committee. Patients participating in another intervention study prior to randomization will not be randomized.

1.6.3 Sequence of Procedures

It is recognized that Clinical Center Institutional Review Boards (IRBs) have official responsibility for determination of informed consent procedures. Prototype informed consent forms have been developed for the study, and each Clinical Center's IRB-approved consent form will be reviewed to make sure the essential material is included. The following description is intended as a guideline that most centers could follow.

The consent form should include the three stages of the study. 1) Consent should be obtained at the time of the Screening Visit, and will include description of the interaction with members of the study team, measurement of complete physical examination, blood and urine tests. 2) Consent for Baseline Period will include consent to interact with members of the study team; control of blood pressure to the pre-randomization goal; assessment of GFR and compliance; compliance with study procedures; and intention to agree later to follow the regimen selected by random assignment. 3) Consent for the Follow-Up Period will include in addition to the above specific consent to be randomized to a treatment regimen, and consent to randomization to one of two blood pressure goal ranges. Consent for the other stages of the study may be obtained separately or combined into a single form.

1.6.4 Privacy

At the beginning of the study, each participant is assigned an identification number and a name code. Participants are identified only by number in any individual tabulations, and it is expected that only group data will be published. If individual participant data are published, no identifying information will be included. The medical records of participants in the AASK Study will be confidential. Specific study related information may be made available to the Food and Drug Administration, the study sponsors, and National Institutes of Health.

1.7 Evaluation of Recruitment and Compliance

Screening forms have been designed to provide information on the success rates (yields) of the various recruitment strategies. All forms used in the study are coordinated to provide information on the retention rates of recruited and randomized participants and the reasons for drop-out and non-compliance with the prescribed regimen. These data will be analyzed during Phase III of the Pilot Study in order to inform the Steering and Planning Committee and the External Advisory Committee for planning the Full-Scale Trial.