CHRONIC RENAL INSUFFICIENCY COHORT (CRIC) STUDY

Sponsored by the National Institutes of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Department of Health and Human Services (DHHS)

AMENDMENT #1
DATED: March 17, 2003

FINAL PROTOCOL VERSION 1.0
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CRIC STUDY PROTOCOL - AMENDMENT #1

The changes listed below have been proposed to the CRIC Study Protocol, Version 1.0, Dated January 13, 2003. These changes have been approved by the Principal Investigators and Steering Committee. Upon approval by the Institutional Review Board a new version of the CRIC Study Protocol, Version 1.1 and new effective date will be implemented.

1. **EXCLUSION CRITERIA:**

   A. **Eliminate the following criterion:** Life expectancy less than 3 years as judged by the site investigator.

   Replace with the following statement: Participant appears unlikely or unable to participate in the required study procedures as assessed by the investigator, study coordinator or designee.

   B. Presently states: Currently participating in an interventional clinical trial (i.e., primarily trials of therapeutic agents that may have an effect on renal or cardiovascular outcomes as assessed by a Central Adjudication Committee)…

   Add the following text: …or in a research study that adds significantly to the participant's burden. Examples of studies that would preclude participation in CRIC are the AASK Cohort or KEEP Study.

   Location: Section 3.C.5. Exclusion Criteria, p. 25.

2. **LIPID TESTS**

   Total cholesterol, triglycerides, HDL and LDL cholesterol will be obtained annually as part of the core study. This change represents the addition of HDL and LDL cholesterol tests.

   Location: Section 3.D.4 Biochemical Measures, p. 40 and Appendix F.

3. **REVISED LIST OF LABORATORY TESTS**

   Biochemical measures are described in Section 3.D.4 and listed in Appendix F of the protocol. Minor changes have been made to the collection schedule of several tests.

   Location: Section 3.D.4 Biochemical Measures, p. 40 and Appendix F.

4. **REPORTING ECG RESULTS**

   The present protocol includes distribution of ECG study results to the primary care physician within 4 – 6 months of the study. However, central reading of the ECG has been deferred until later in the study. The following reporting schedule will be employed:

- Local readings within 24 hours to evaluate for the following urgent conditions: bradycardia < 45 bpm, tachycardia > 120 bpm, acute myocardial infarction or ischemia, ventricular tachycardia, atrial fibrillation, atrial flutter, Mobitz Type II 2nd degree heart block and 3rd degree heart block, complete left bundle branch block.
- Central clinical reading is deferred until later in the study (Year 4 or later).

- Change of frequency for ECG testing from Baseline and Year 4 to annual ECG testing, which will be conducted during the participant's annual clinical visit and stored for future analysis.

Location: Section 4.B.1. Transmission of Study Findings and Response Time, p. 54 and Appendix D.

5. BLOOD PRESSURE MEASURES

Blood pressure measures described in the present protocol state that mean arterial pressure and pulse pressure will be calculated. This procedure has been changed as follows: Blood pressure will be measured at the Screening Visit, repeated at the Baseline Visit and annually thereafter. The procedure involves taking three sequential measurements while the participant is seated followed by one measurement while standing.

Location: Section 3.D.1 Physical Measures, p. 27 and Visit Schedule Appendix A.

6. STUDY ORGANIZATION – CLINICAL CENTERS

The principal investigator at the Case Western Reserve University has been changed. Mahboob Rahman, MD, will serve as the investigator instead of Jackson T. Wright, Jr., M.D., Ph.D.

Location: Section 5.A.Clinical Centers, p. 59.

7. VISIT SCHEDULE – APPENDIX A

The following changes have been made:

- Adjustment (reduction) in the administration frequency of several questionnaires resulting in a reduced participant burden.
- Blood pressure measured at the screening visit in addition to the baseline visit.
- BIA measured at baseline and alternate years, originally measured annually
- Permit 3 month interval between screening and baseline visit. [Formerly 45 days]
- Permit combination of the screening and baseline visits to suit participant convenience, provided the necessary eligibility serum creatinine value and estimated GFR calculation are confirmed.

Location: Section 3.C.6. Participant Procedures, p. 26 and Appendix A.

8. **ANCILLARY STUDIES**

The listing of proposed ancillary studies will be deleted and replaced with the following policy statement regarding the appropriate review and assessment of integration into the CRIC core study.

Policy

To enhance the value of the CRIC Study, the Steering Committee welcomes proposals from individual investigators to carry out ancillary studies. Nevertheless, to protect the integrity of the CRIC Study, such ancillary studies must be reviewed and approved by the Primary and Ancillary Studies Committee and the Steering Committee before submission of a proposal for external funding consideration.

Definition of Ancillary Study

An ancillary study is one based on information from CRIC Study participants in an investigation or analysis which is relevant to, yet not described in the CRIC Study protocol, and derives support from non-CRIC Study funds. A typical ancillary study will propose the collection of additional data not collected or analyzed as part of the routine CRIC Study data set. Ancillary studies may be submitted by the investigators within the CRIC Study or by investigators without a prior relationship to the CRIC Study. Ancillary studies require external (non-CRIC Study) funding. Examples include studies funded by investigator-initiated NIH research awards (R series awards, K series awards, and other career development 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 CRIC Study Clinical Centers and Laboratories (e.g., to process or ship samples), and by the Scientific and Data Coordinating Center.

Considerations for Approval

A. The proposed study must meet requirements of the highest scientific merit.

B. Participant burden:
   1. The proposed study must be acceptable to the participants (e.g. time, discomfort, privacy).
   2. The proposed study must not interfere with other parts of the main CRIC Study.
   3. The proposed study must not hamper continued participation in the main Study.
   4. The proposed study must put minimal demand on scarce CRIC Study resources such as blood samples.

C. The proposed study must require the unique characteristics of the CRIC Study cohort to accomplish its goals.

D. The investigators must have adequate resources to effectively complete the project, including:
   1. Sufficient budget and personnel
   2. Staff having the requisite expertise to meet the objectives of the project.

E. The ancillary study investigators must agree to return the complete ancillary data set back to the CRIC Study if requested by the CRIC Study Steering Committee.

F. The proposed study must not interfere with the completion of the main objectives of CRIC Study.

G. The proposed study must not adversely affect participant cooperation or compliance with CRIC Study.

H. The proposed study must not create a serious diversion of study resources (personnel, equipment or study samples) or investigator/staff time, either locally or centrally.

I. The proposed study must not jeopardize the public image of the CRIC Study.

J. The proposed study must document involvement of the CRIC investigators as part of the research team.

Location: Appendix C.

APPENDIX A

CRIC Visit Schedule – Revised 3/17/2003	Pre-Screen	Screen-ing	Base Line	6 Mos.	12 Mos.	18 Mos.	24 Mos.	30 Mos.	36 Mos.	42 Mos.	48 Mos.	54 Mos.	60 Mos.
Type of Contact	**Phone**	**Visit**	**Visit**	**Phone**	**Visit**	**Phone**	**Visit**	**Phone**	**Visit**	**Phone**	**Visit**	**Phone**	**Visit**
Eligibility Assessment	X												
Informed Consent		X											
Medical Record Consent		X			X		X		X		X		X
Contact Information		X		X	X	X	X	X	X	X	X	X	X
Labs: Serum creatinine, glucose		X											
Demographic Information		X											
Eligibility Confirmation		X	X										
Medical History [CV, renal, health behaviors]			X		X		X		X		X		X
Genetic Blood Sample			X		X		X		X		X		X
Labs: CBC, metabolic panel, lipids, etc.			X		X		X		X		X		X
Urinary Assay: 24 Hour Urine [creatinine, protein, albumin, urea nitrogen]		X	X		X		X		X		X		X
Blood Pressure		X	X		X		X		X		X		X
Ankle Brachial Index & Anthropometric Measures			X		X		X		X		X		X
Bioelectrical Impedance Assessment [BIA]			X				X				X		
Toenail Clippings			X		X		X		X		X		X
ECG			X		X		X		X		X		X
Echocardiogram					X						X		
EBT (1/3 Participants)					X						X		
I-GFR (1/3 Participants)			X				X				X		
Physical Activity Assessment			X				X				X		
Concomitant Medications			X	X	X	X	X	X	X	X	X	X	X
MDRD Symptom Index			X		X		X		X		X		X
KDQOL - Quality of Life Questionnaire			X		X		X		X		X		X
Diet History Questionnaire			X				X				X		
Beck Depression Inventory			X				X				X		
Cognitive Function Testing [Mini Mental Status Exam]			X				X				X		
Recent Medical History – Event Information				X	X	X	X	X	X	X	X	X	X