Manuscript #027B

1. Title:
(Full): Association of high LDL-C with clustering of metabolic abnormalities
(Abbrev.): ASSOCIATION OF LDL-C WITH MMS CLUSTERING

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3. Timeline:
All analyses should be completed and a new draft paper circulating within the next few months

4. Rationale:
(Two ARIC manuscripts (MS#27 and MS#27A) have investigated the clustering of metabolic abnormalities hypertension, diabetes, hypertriglyceridemia, low HDL-C and hyperuricemia among participants at baseline. In the initial analyses, LDL-C was included in the definition of clustering. However, due to journal referee comments, in spite of some evidence of LDL-C clustering, LDL-C was removed from the manuscripts. The Publications Committee approved presentation of additional analyses dealing with the extent and nature of the association between high LDL-C and clustering of the other above-mentioned abnormalities at the American Diabetes Association meetings, which occurred this month. This request thus basically aims to formalize a separate AWG number for these analyses.)

Perhaps because the existing pathophysiologic evidence suggests that insulin resistance is not associated with high LDL-C, little work has been done on a population basis to investigate the association of high LDL-C with clustering of dyslipidemia, diabetes, hypertension and hyperuricemia. Though in retrospect perhaps guided by a misunderstanding of what was known about this clustering, initial AWG#27 analyses showed a clinical significant association between the presence of high levels of LDL-C and clustering of the other metabolic abnormalities, especially in white women.

5. Main Objective:
To document the presence of an association between high LDL-C and clustering of abnormalities linked to the multiple metabolic syndrome, and to investigate gender and ethnic variability in this clustering. In an attempt to better understand this phenomenon, to investigate variability in the association by menopause status in women, and additionally the association of the individual abnormalities composing the clusters with high LDL-C.

6. Data:
Basically the same data as used in the MS #027 analyses: hypertension, diabetes, triglycerides, HDL-C,
uric acid, fasting insulin, WHR, BMI, gender, ethnicity, fasting time, insulin, age at visit one; LDL-C and menopause status.