



## Educational Discussion: Lipoprotein(a) Testing

### 2020-A Accuracy-Based Lipids (ABL)

Measurement of traditional lipids (total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides) has represented one cornerstone in cardiovascular disease risk (CVD) assessment for decades. However, it has been found that these traditional lipids leave a considerable proportion of high risk patients undetected. At the same time, limitations in the measurement of traditional blood lipids were better defined in research studies and have been confirmed in findings made in the ABL Surveys. For example, the effect of triglyceride levels on measurement accuracy of LDL-cholesterol and HDL-cholesterol were pointed out in previous ABL Participant Summary Reports.

This situation stimulated research for new CVD risk biomarkers to supplement traditional blood lipids or as alternatives for them. Findings from this research are reflected in recent guidelines [1,2,3] stating that measurement of Lp(a) is considered to be a risk-enhancing factor and apolipoprotein B might be of advantage in patients with hypertriglyceridemia. Specifically, the ACC/AHA guidelines mention cut-off values for Lp(a) ( $>50$  mg/dL or  $>125$  nmol/L) and apolipoprotein B ( $\geq 130$  mg/dL) as part of primary prevention in certain subgroups of patients. To apply these suggested cut-off values consistently, measurements of these lipoproteins need to be accurate.

The ABL Survey provides commutable, high quality sera that allow the assessment of measurement comparability across assay systems. In addition, it provides target values determined with highly precise and accurate reference measurement procedures. This enables the assessment of measurement accuracy performed by laboratories and among peer groups. This Survey provides for the first-time target values for Lp(a) obtained using a mass spectrometry method. This method is part of the work conducted by International Federation of Clinical Chemistry to standardize lipoprotein measurements.

Lp(a) is an LDL-like particle with 1 molecule of apoB to which an additional apolipoprotein, apo(a), is covalently attached. This apolipoprotein consists of a unique amino acid sequence section and an amino acid sequence that is repeated (so called 'kringle IV type 2 (KIV-2) repeats'). There is considerable (over 1,000 fold) variability in the number of KIV-2 repeats among individuals [4]. As a result, the amount of Lp(a), expressed in 'mg/dL', can represent very different numbers of proteins. Therefore, results reported in 'mg/dL' that assume an average molecular weight for Lp(a) may not match with results reported in 'nmol/L'. Lp(a) is currently not standardized and efforts to standardize Lp(a) measurements and reporting of results are under way. In this Survey, Lp(a) was determined using the non-repeat section of the protein and is expressed in 'nmol/L'. Therefore, the target values are independent of the size of the molecule.

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### References:

1. Arnett et al. Circulation. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. 2019;140:e563–e595
2. Grundy et al. 2018  
AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the



management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139:e1082–e1143.

3. Piepoli et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. *European Heart Journal* 2016; 37:2315–2381
4. Langlois et al. Quantifying Atherogenic Lipoproteins: Current and Future Challenges in the Era of Personalized Medicine and Very Low Concentrations of LDL Cholesterol. A Consensus Statement from EAS and EFLM. *Clin Chem*. 2018;64:1006-1033