ClevelandHeartLab®
Know your risk.

May 10th, 2016

Dear Valued Cleveland HeartLab Customer,

Thank you for your ongoing commitment to delivering the latest advances in cardiovascular risk assessment from Cleveland HeartLab to your patients. We are honored to be your partner in the identification and prevention of CVD. As you know, Cleveland HeartLab is a science-driven company and the creator of the multi-marker approach to cardiovascular risk identification utilizing Inflammation Testing.

As the leader in Inflammation Testing, Cleveland HeartLab is always looking for ways to improve our test offering through our industry-leading R&D program. As a result, we are introducing a change to the Lp-PLA_2 assay test offered by Cleveland HeartLab.

Currently, Cleveland HeartLab performs the Lp-PLA_2 (The PLAC® Test) assay which measures the concentration (or "mass") of Lp-PLA_2. **Beginning Monday, May 23rd, 2016, Cleveland HeartLab will begin performing an internally developed and validated Lp-PLA_2 Activity assay, and discontinue the use of the Lp-PLA_2 Concentration ("mass") assay.**

Important information about Cleveland HeartLab's new Lp-PLA_2 Activity assay:

- This test was developed as a result of the well-documented clinical utility of Lp-PLA_2 Activity in the literature to assess risk of CHD[1].
- This test will be run on LC/MS/MS technology and will improve the quality and consistency of results due to enhanced analyte and assay stability.
- The results from this new test will have different reporting ranges than the current Lp-PLA_2 Concentration ("mass") assay you are getting from Cleveland HeartLab.
- As a result of the differences in reporting ranges, when comparing new test results to previous test results, Cleveland HeartLab will provide historical relative risk results (i.e. High or Low) for Lp-PLA_2 Concentration ("mass") when the Lp-PLA_2 Activity test is resulted.
- There are no changes to the sample type, CPT code, or CHL EasyPay amount.
- **All requisition forms received on or after Monday, May 23rd requesting an Lp-PLA_2 test will automatically be converted to the Lp-PLA_2 Activity assay.**

On the following pages are answers to some important commonly asked questions regarding conversion from the Lp-PLA_2 Concentration ("mass") assay to the Lp-PLA_2 Activity assay.

If you have questions or would like more information, please contact our educational team at consult@clevelandheartlab.com.

Kind Regards,

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Medical Director and VP of Laboratory Operations

Marc S. Penn, MD, PhD, FACC
Chief Medical Officer

[1]The Lp-PLA_2 Studies Collaboration. Lipoprotein-associated phospholipase A2 and risk of coronary disease, stroke, and mortality: Collaborative Analysis of 32 prospective studies. *Lancet*. 2010; 375: 1536-1544.

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Conversion from the **Lp-PLA$_2$ Concentration ("mass") assay** to the CHL **Lp-PLA$_2$ Activity assay**

1) Why is Cleveland HeartLab converting to an Lp-PLA$_2$ Activity assay?
Recent literature demonstrates that measuring Lp-PLA$_2$ Activity translates into improved accuracy of results as well as increased analyte stability. This ultimately translates into improved performance and efficiencies for you.

2) Did the assay methodology change?
Yes. The Lp-PLA$_2$ Concentration ("mass") assay utilizes an ELISA platform, and the new Lp-PLA$_2$ Activity assay utilizes LC/MS/MS technology.

3) Are the clinical cut-offs different between Cleveland HeartLab's Lp-PLA$_2$ Activity assay and those reported by DiaDexus's The PLAC® Test?
Yes. The cut-offs between the two assays are different as they are measuring two fundamentally different aspects of the Lp-PLA$_2$ analyte, and utilize different methodologies.

Lp-PLA$_2$ Assay	Cut-Off		Methodology
	Low	High	
Cleveland HeartLab's Lp-PLA$_2$ Activity assay	<75 nmol/min/mL	≥75 nmol/min/mL	LC/MS/MS
DiaDexus's The PLAC® Test	≤200 ng/mL	>200 ng/mL	ELISA

4) Can the Lp-PLA$_2$ Concentration ("mass") results and Lp-PLA$_2$ Activity results be used interchangeably?
No. They are measuring two fundamentally different aspects of the Lp-PLA$_2$ analyte. One assay measures concentration ("mass"; ng/mL) and the other measures the enzyme activity of the Lp-PLA$_2$ protein (nmol/min/mL).

5) Will the conversion from the Lp-PLA$_2$ Concentration ("mass") assay to an Lp-PLA$_2$ Activity assay affect historical reporting?
Yes. Cleveland HeartLab will only provide historical relative risk results (i.e. High or Low) for Lp-PLA$_2$ Concentration ("mass") when the Lp-PLA$_2$ Activity test is resulted.

Comparison of **Cleveland HeartLab's LDT Lp-PLA$_2$ Activity assay** to DiaDexus's **Lp-PLA$_2$ Activity assay**

1) Does Cleveland HeartLab's Lp-PLA$_2$ Activity assay results correlate with those obtained by DiaDexus's Lp-PLA$_2$ Activity assay?
Yes. Results obtained from Cleveland HeartLab's Lp-PLA$_2$ Activity assay correlate extremely well with DiaDexus's Lp-PLA$_2$ Activity assay (r=0.96).

2) Do results from Cleveland HeartLab's Lp-PLA$_2$ Activity assay and DiaDexus's Lp-PLA$_2$ Activity assay provide the same clinical utility?
Yes. Despite different numerical values, the results provide the same clinical information regarding categorizing individuals into low or high risk categories.