### Oxidized LDL - A Powerful Tool for Clinical Diagnostics

#### What is Oxidized LDL?

LDL, the "bad cholesterol", can be modified (i.e., oxidized) and it is this modified form that is responsible for atherosclerotic plaque formation.

Oxidized LDL, but not LDL, is recognized and taken up

by scavenger receptors on macrophages in the arterial wall and it is the accumulation of oxidized LDL that converts these macrophages into the catastrophic foam cells, a hallmark of atherosclerosis. As this pro-



cess continues, more and more foam cells are formed leading to a clumping effect and plaque formation.

As these plaques build up in arteries, the lumen is narrowed and blood flow is progressively restricted. Partial or full occlusions can have devastating consequences (e.g., tissue death) and are often fatal. A vulnerable plaque is one that has an increased susceptibility for complications, often manifesting in a rupture and subsequent thrombosis. Acute trauma due to vulnerable plaque constitutes a large portion of cardiovascular-related deaths.

#### Oxidized LDL as a Biomarker

The prevalence of metabolic diseases has been steadily increasing in populations across the globe. This has had a significant impact on quality of life and health care costs. Biomarker measurements are an integral part of patient evaluations during routine examinations, including assessments of acute and chronic conditions.

In a study of over 136,000 coronary artery disease (CAD) hospitalizations at hundreds of hospitals, approximately 50% of those patients had LDL <100 mg/dL and 17.6% of patients had LDL <70 mg/dL, at admission. Less than 1/3 of the patients had LDL >130 mg/dL.<sup>1</sup>

Better biomarkers are needed for prediction, diagnosis, treatment and monitoring!

Hundreds of publications (using the **Mercodia Oxidized LDL ELISA**) have established and confirmed the role of oxidized LDL in cardiovascular disease and its association with other conditions (e.g., obesity, diabetes, PCOS, etc.). The positive correlation between blood levels of oxidized LDL and % of patients with CAD (Figure 1a) has been shown to be much stronger than the correlation between LDL and % of patients with CAD (Figure 1b).<sup>2</sup>

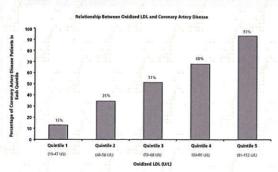


Figure 1a.

Elevated oxidized LDL levels can signify that increased oxidative stress and inflammation in the body have led to protein modifications involved in disease processes. This is an indication that deleterious physiological changes are occurring. Therefore, many in the clinical diagnostics field have chosen to go a step further with their evaluation of health by including oxidized LDL in patient assessments.

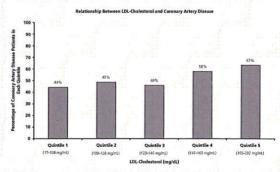
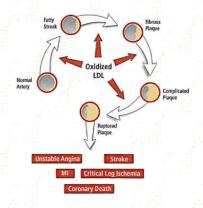


Figure 1b.



#### Use of Oxidized LDL by Healthcare Professionals

Healthcare professionals have used oxidized LDL to assess patient health in various clinical settings. There are multiple ways in which this valuable biomarker can be used.

Oxidized LDL is often used as a stand alone measure due to its role in the initiation and progression of atherosclerosis. Oxidized LDL is also included in select biomarker panels in order to provide a more comprehensive understanding of patient health. Oxidized LDL to HDL cholesterol ratio is the most superior blood lipid test for discriminating between healthy controls and CAD-patients.

Determining metabolic syndrome risk has become increasingly important as it is linked to numerous devastating health conditions and increased mortality from cardiovascular disease. In a large population-based study published in *JAMA*, increased oxidized LDL was associated with a significant increased risk of developing metabolic syndrome, even after adjusting for other key factors such as LDL.



The authors concluded that "the strong association of oxidized LDL with the incidence of metabolic syndrome is consistent with a causal role".

Furthermore, elevated levels of oxidized LDL were associated with an increased risk of incident myocardial infarction (MI), suggesting an effect of oxidized LDL on MI independent of the metabolic syndrome, adding prognostic information concerning future risk for MI.<sup>3</sup>

#### Treating Patients with High Oxidized LDL Levels

The value of biomarkers in the medical field is significant because they provide healthcare professionals the ability to intervene with strategies to reduce risk and optimize health.

Many studies have been published (using the **Mercodia Oxidized LDL ELISA**) showing decreases in oxidized LDL after various lifestyle and pharmacological interventions. Please contact Mercodia for more information about these studies and an updated reference list.

# Special Populations - Children and Adolescents

In 2011, the NIH Heart, Lung and Blood Institute (NHLBI) recommended universal cholesterol screening between the ages of 7-11 and again between ages 17 and 21, highlighting the importance of monitoring the cardiovascular health of this unique population.

Overweight and obese children as young as six years of age have been found to have elevated levels of oxidized LDL, a startling indication of early signs of atherosclerosis.<sup>4</sup> Oxidized LDL can provide additional evidence of the need for interventions to prevent future complications in children and adolescents.



The **Mercodia Oxidized LDL ELISA** is the most well-characterized oxidized LDL measurement method and is based on the highly specific 4E6 monoclonal antibody. Developed by a world leader in ELISA technology, this assay has excellent performance characteristics.

The **Mercodia Oxidized LDL ELISA** has been used in hundreds of publications, including many large scale clinical trials, and is used routinely for clinical diagnostic purposes.

- High precision
- Excellent repeatability and reproducibility
- Easy-to-automate protocol
- Optimized to minimize handling errors

#### **Frequently Asked Questions**

What types of patient samples can be used?\*

Serum

EDTA plasma

Heparin plasma

Citrate plasma

\*Reference labs may have their own requirements or preferences.

#### Is it ok if samples have been frozen?

While it is always optimal to use fresh samples, Mercodia has conducted stability studies and found no significant changes in oxidized LDL levels with as many as five freezethaw cycles.

## Can samples be used if they have been stored for a long period of time?

Yes. Oxidized LDL levels in serum, EDTA plasma and heparin plasma are stable for at least three years at -70°C or below.<sup>5</sup>



#### What are the reference ranges for oxidized LDL?

Reference ranges must always be established and reported by the clinical reference lab used. Examples of references ranges used by one CLIA certified lab are provided below.

| Oxidized LDL (U/L) |                | LDL/HDL (U/mmol) |                |
|--------------------|----------------|------------------|----------------|
| <45                | low risk       | <35              | low risk       |
| 45-59              | moderate risk  | 35-51            | moderate risk  |
| 60-79              | high risk      | 52-74            | high risk      |
| >79                | very high risk | >74              | very high risk |

#### NOTE:

Mercodia's Oxidized LDL ELISA is CE and IVD marked. This assay is listed with the FDA as a Class I IVD device.





#### References

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- 1. Sachdeva et al. (2009) Am Heart J 157:111-117.e2.
- 2. Johnston et al. (2006) Am J Cardiol 97:640-645.
- 3. Holvoet et al. (2008) JAMA 299:2287-2293.
- 4. Kelly et al. (2010) Pediatr Diabetes 11:552-555.
- 5. Perman et al. (2004) Scand J Clin Lab Invest 64:753-756.

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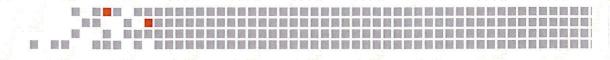
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