



**PDA publishes Technical Report No. 82 on
Low Endotoxin Recovery (LER), including case study with
ENDO-RS® Endotoxin Recovery Method by
Hyglos - a bioMérieux company.**

In March 2019, the Parenteral Drug Association (PDA) published Technical Report No. 82 (TR82) on Low Endotoxin Recovery (LER). The report constitutes a much needed source of information and guidance, including scientific findings on mechanism, data on clinical relevance, as well as recommended procedures for analysis and mitigation of endotoxin masking commonly leading to LER in biologics. This comprehensive document is a result of three years intensive work by the PDA LER Task Force, which consists in members from U.S. FDA, academia, pharmaceutical industry and endotoxin testing suppliers.

An important part of TR82 is the comprehensive appendix of case studies considering LER occurrences. This section encompasses both analyses of root-causes and endotoxin preparations, as well as methodologies for overcoming LER. In one of the studies, Case Study 7: Evaluation of an Endotoxin Demasking Protocol, the application of the ENDO-RS methodology developed by Hyglos was assessed. This study used a sample known to be affected by LER to develop a sample preparation protocol using ENDO-RS reagents prior to detection of endotoxin using the LAL method. The results showed that the resulting ENDO-RS protocol was able to reliably detect the endotoxin under all conditions tested, ensuring robust recovery and diminishing the risk of false-negative test results.

To read the case study and PDA Technical Report No. 82 in full, it is available for members and can be purchased directly from the PDA Technical Reports Portal:
<https://www.pda.org/publications/pda-publications/pda-technical-reports>

ABOUT LOW ENDOTOXIN RECOVERY (LER)

First reported by Chen and Vinther in 2013, the phenomenon known as Low Endotoxin recovery (LER) has been broadly studied and identified in biologics and certain therapeutic proteins. LER is a temperature- and time-dependent process and defined as loss of detectable endotoxin activity over time when using Factor C-based assays (LAL and rFC) when undiluted products are spiked with known amount of endotoxin standards. Since 2013, regulatory authorities also request hold-time studies to determine the validity of the endotoxin release test methods during the review of BLAs for biotech products, as well as new methods to overcome the issue.

ABOUT ENDO-RS® ENDOTOXIN RECOVERY KIT

The ENDO-RS® method developed by Hyglos - a bioMérieux company, is a unique toolbox for sample preparation addressing masking of endotoxin in biopharmaceutical formulations containing surfactants and chelating agents. ENDO-RS® enables full quantitative recovery of endotoxin independent of storage time and endotoxin concentration.



ABOUT ENDOXPERTS™ ENDOTOXIN SERVICES BY BIOMÉRIEUX

Our ENDOXPERTS™ Endotoxin Services unit offers routine testing and feasibility studies as well as specialized method development services for analytical challenges such as Low Endotoxin Recovery (LER) applying our patented ENDO-RS® technology. Our work for leading pharmaceutical companies has resulted in validated methods for LER, fulfilling regulatory requirements. Applying true scientific soundness, we continue our contribution to the deepened knowledge of the LER phenomenon and complex nature of endotoxin.

ABOUT BIOMÉRIEUX

Pioneering Diagnostics

A world leader in the field of *in vitro* diagnostics for more than 50 years, bioMérieux is present in more than 150 countries through 42 subsidiaries and a large network of distributors. In 2016, revenues reached € 2,103 million, with over 90% of international sales.

bioMérieux provides diagnostic solutions (systems, reagents, software) which determine the source of disease and contamination to improve patient health and ensure consumer safety. Its products are mainly used for diagnosing infectious diseases. They are also used for detecting microorganisms in agri-food, pharmaceutical and cosmetic products.



bioMérieux is listed on the Euronext Paris stock market

Symbol: BIM - ISIN Code: FR0013280286

Reuters: BIOX.PA/Bloomberg: BIM.FP

Corporate website: www.biomerieux.com.

Industry Website : www.biomerieux-industry.com/