2017 PDA Endotoxins Workshop  
October 18-19, 2017 | Bethesda North Marriott Hotel & Conference Center | Bethesda, MD 
<As of September 25, 2017>

Wednesday, October 18

11:30 a.m.-5:30 p.m.  
Registration Open

1:15 p.m.-1:30 p.m.  
Welcome and Opening Remarks from Conference Co-Chair  
Jennifer Farrington, PhD, Associate Director, Regulatory Affairs, Associates of Cape Cod, Inc.

1:30 p.m.-3:30 p.m.  
P1: Opening Plenary: Academic Perspectives on the Limulus Amebocyte Lysate Assay and Endotoxin Structure and Diversity  
Moderator: Jessica V. Hankins, PhD, Microbiology Reviewer, CDER, FDA

**Session Description:** The Limulus Amebocyte Lysate (LAL) assay is the standard test method used to detect endotoxin in pharmaceutical products and medical devices. Although the overall biosynthesis of endotoxin is well conserved among Gram-negative bacteria, many organisms possess quite diverse endotoxin structures. This session will highlight the discovery and background of the LAL test and standardization of the lysate and reference standard endotoxin used in bacterial endotoxin testing. Additionally, this session will give attendees a broad overview of endotoxin biosynthesis, the structural diversity of endotoxins, and the mechanisms which regulate this enzymatic machinery.

1:30 p.m.-2:15 p.m.  
The Limulus Amebocyte Lysate (LAL) Test: Discovery, Development & Applications  
Jack Levin, MD, Professor of Laboratory Medicine, University of California, San Francisco

2:15 p.m.-3:00 p.m.  
How Gram-Negative Bacteria Harden Their Armor: Diversity of Endotoxin Structure  
M. Stephen Trent, PhD, Professor, Department of Infectious Diseases, The University of Georgia

3:00 p.m.-3:30 p.m.  
Questions and Answers/Discussion

3:15 p.m.-7:30 p.m.  
Exhibit Area Open

3:30 p.m.-4:15 p.m.  
Refreshment Break in Exhibit Area

4:15 p.m.-6:15 p.m.  
P2: Practical Issues with Endotoxin Testing and Regulatory Responsibilities of Sponsors  
Moderator: Allen L. Burgenson, MS, Manager, Regulatory Affairs, Lonza Walkersville, Inc.

**Session Description:** This session will provide the attendee with the regulatory responsibilities of sponsors filing New Drug Applications (NDAs) or Biologics License Applications (BLAs) applications with U.S. FDA, and practical testing information.

4:15 p.m.-4:45 p.m.  
FDA Case Studies: Problems and Solutions… or Problems and More Problems  
Maria “Reyes” Candau-Chacon, PhD, Biologist, CDER, FDA

4:45 p.m.-5:15 p.m.  
Determining Endotoxins Limits for Raw Materials and APIs  
Amber Dellar, Senior Operational Excellence Specialist, Pfizer Inc.

5:15 p.m.-5:45 p.m.  
Horseshoe Crabs and the Limulus Test: The Blue Bloods of Parenteral Quality Control  
John A. Dubczak, General Manager Endotoxin and Microbial Detection, Charles River Laboratories, Inc.

5:45 p.m.-6:15 p.m.  
Questions and Answers/Discussion

6:15 p.m.-7:30 p.m.
Networking Reception in Exhibit Area

Thursday, October 19

7:00 a.m.-4:30 p.m.
Registration Open
7:00 a.m.-8:30 a.m.
Continental Breakfast

7:15 a.m.-8:15 a.m.
Breakfast Session: Data Integrity
Moderator: Jennifer Farrington, PhD, Associate Director, Regulatory Affairs, Associates of Cape Cod, Inc.

Session Description: This session will provide the latest regulatory perspective on Data Integrity and Part 11 compliance specific to endotoxin testing. We will cover why it is a concern to the Regulatory authorities and areas of concern during Limulus Amebocyte Lysate (LAL) testing.

7:15 a.m.-7:45 a.m.
Douglas W. Stearn, JD, Director, Office of Enforcement and Import Operations, ORA, FDA
7:45 a.m.-8:15 a.m.
Questions and Answers/Discussion

8:30 a.m.-10:00 a.m.
Moderator: Jessica V. Hankins, PhD, Microbiology Reviewer, CDER, FDA

Session Description: Beta-glucans are large polysaccharides found in the cell walls of various eukaryotic and prokaryotic organisms. These polysaccharides possess immunostimulatory properties and are potential contaminants of parenteral drugs and medical devices. This session will focus on the structure (1→3)-β-D-glucan, its sources as a contaminant, its effect on LAL-based endotoxin testing, mitigation approaches, and potential impact to patient safety.

8:30 a.m.-9:00 a.m.
(1→3)-β-D-Glucan: Properties, Sources, Bacterial Endotoxins Test Interference, and Mitigation Strategies
Malcolm A. Finkelman, PhD, Director, Clinical Development, Associates of Cape Cod, Inc.
9:00 a.m.-9:30 a.m.
Parenteral Safety of Beta-Glucans
Christine Schubert, PhD, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Basel
9:30 a.m.-10:00 a.m.
Questions and Answers/Discussion

9:45 a.m.-4:15 p.m.
Exhibit Area Open
10:00 a.m.-10:45 a.m.
Refreshment Break in Exhibit Area
10:45 a.m.-12:50 p.m.
Concurrent Sessions

Attendees will participate in both breakouts, each 60 minutes long. After Session 1, attendees will switch and the breakouts will be repeated.
Session 1: 10:45 a.m. – 11:45 a.m. | Session 2: 11:50 a.m. – 12:50 p.m.

Session 1

<table>
<thead>
<tr>
<th>Group A – Case Study 1: Setting Endotoxin Specifications</th>
<th>Group B – Case Study 2: Setting in-Process Endotoxin Limits</th>
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<tbody>
<tr>
<td>Moderator: Jay Bolden, Associate Senior Consultant Biologist, Global Quality Laboratories, Eli Lilly and Company</td>
<td>Moderator: Friedrich von Wintzingerode, PhD, Senior Manager Microbiology, Roche Diagnostics GmbH</td>
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<td>Session Description: Endotoxin specification calculations for injectable drug products are harmonized in the major compendia. This session will present a case study and give participants the opportunity to create a drug product and drug substance endotoxin specification control strategy, while</td>
<td>Session Description: There is a lack of detailed guidance for setting endotoxin in process limits (alert levels and action limits) for biologics. This session will present a case study which allows participants to understand the underlying rationales and challenges. Aspects of method alignment between different</td>
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mitigating for unusual circumstances and balancing considerations for patient safety, the threshold pyrogenic dose constant, analytical and process capabilities, and reliable market supply.

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<tbody>
<tr>
<td>10:45 a.m.-11:05 a.m.</td>
<td>Review of Case Study</td>
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<tr>
<td>11:05 a.m.-11:25 a.m.</td>
<td>Small Group Discussion</td>
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<tr>
<td>11:25 a.m.-11:45 a.m.</td>
<td>Group Reports</td>
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Session 2

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<td>12:10 p.m.-12:30 p.m.</td>
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<td>12:30 p.m.-12:50 p.m.</td>
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12:50 p.m.-2:00 p.m.

**Networking Luncheon**

2:00 p.m.-3:30 p.m.

**Small Group Discussion: Pyrogen Test Comparison**

| **Moderator:** Friedrich von Wintzingerode, PhD, Senior Manager Microbiology, *Roche Diagnostics GmbH* |

**Session Description:** During this session, the main difference between the rabbit pyrogen test (RPT) and the monocyte activation test (MAT) on one hand (biological impact of the sample) and the bacterial endotoxins test (BET) on the other hand (quantification of Endotoxin) will be illustrated. The relevance of Non-Endotoxin Pyrogens (NEP) and synergistic effects will be discussed. The legal and regulatory implications of the MAT in Europe and the US will be highlighted.

2:00 p.m.-2:25 p.m.

**Monocyte Activation Test: Industry Perspective**

**Ned M. Mozier, PhD, Senior Director, Pfizer Inc.**

2:25 p.m.-2:50 p.m.

**Monocyte Activation Test: Development**

**Ingo Spreitzer, Deputy Head, 1/3 Microbial Safety, Paul-Ehrlich-Institut**

2:50 p.m.-3:30 p.m.

**Small Group Discussion**

3:30 p.m.-4:15 p.m.

**Refreshment Break in Exhibit Area**

4:15 p.m.-5:45 p.m.

**P4: BET Laboratories: Practical Advice**

| **Moderator:** Jennifer Farrington, PhD, Associate Director, Regulatory Affairs, *Associates of Cape Cod, Inc.* |
Session Description: Whether you use the Bacterial Endotoxin Test to analyze in process materials, finished pharmaceutical drugs, medical devices, biologics or water systems, proper laboratory controls, and understanding of the test is critical to success. This session will explore Limulus Amebocyte Lysate (LAL) test interferences and essential laboratory controls and assay set up. Attendees will leave with practical advice to solve common inhibitory or enhancement problems as well as a more extensive knowledge of areas to look out for when setting up a new laboratory and ongoing review of the existing labs.

4:15 p.m. - 4:45 p.m.
Detection of Endotoxins in Pharmaceutical Operations
John A. Dubczak, General Manager Endotoxin and Microbial Detection, Charles River Laboratories, Inc.

4:45 p.m. - 5:15 p.m.
Laboratory Prerequisites for a Successful Bacterial Endotoxins Test
Veronika Wills, MSc, Associate Manager, Technical Services, Associates of Cape Cod, Inc.

5:15 p.m. - 5:45 p.m.
Questions and Answers/Discussion

5:45 p.m.
Closing Remarks from Conference Co-Chair
Friedrich von Wintzingerode, PhD, Senior Manager Microbiology, Roche Diagnostics GmbH