



# Endotoxin Detection

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# The Problem – Current Tests Inadequate

## PROBLEM:

The current test for endotoxins in parenteral drugs systematically underreports the presence of endotoxin, leading to postmarketing commitments and additional process controls.

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- Chelators and surfactants commonly used in biologics can mask endotoxin in the commonly used LAL assay.
- Low endotoxin recovery (LER) can lead to regulatory delays, including hold-time studies and post-marketing commitments.
- Manufacturing facilities need to account for inhibitory effects on assay results by instituting more stringent process controls.

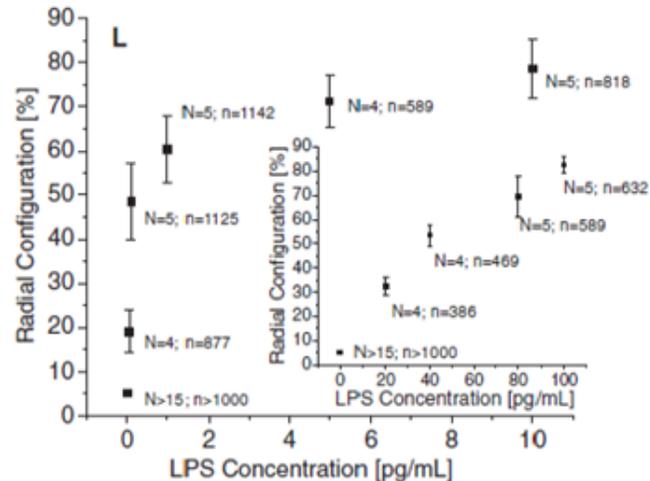
# The Solution - Biophysical Liquid Crystal Tests for Endotoxin

## SOLUTION:

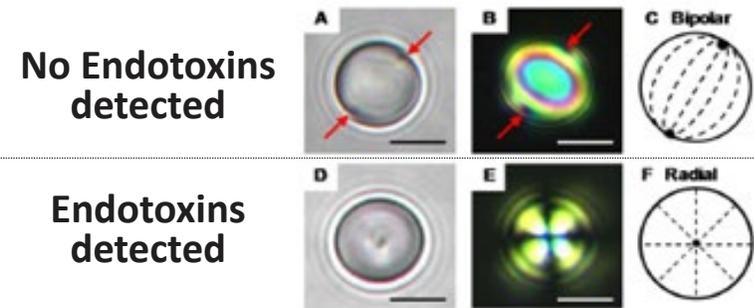
Liquid crystal droplets can be used in a biophysical test to detect the presence of endotoxin.

**Liquid crystals bind to endotoxins and change phase and optical properties.**

- Changes in physical properties (light scattering and transmission of polarized light) can be read with a microscope or flow cytometer.



Liquid Crystals with and without endotoxins detected

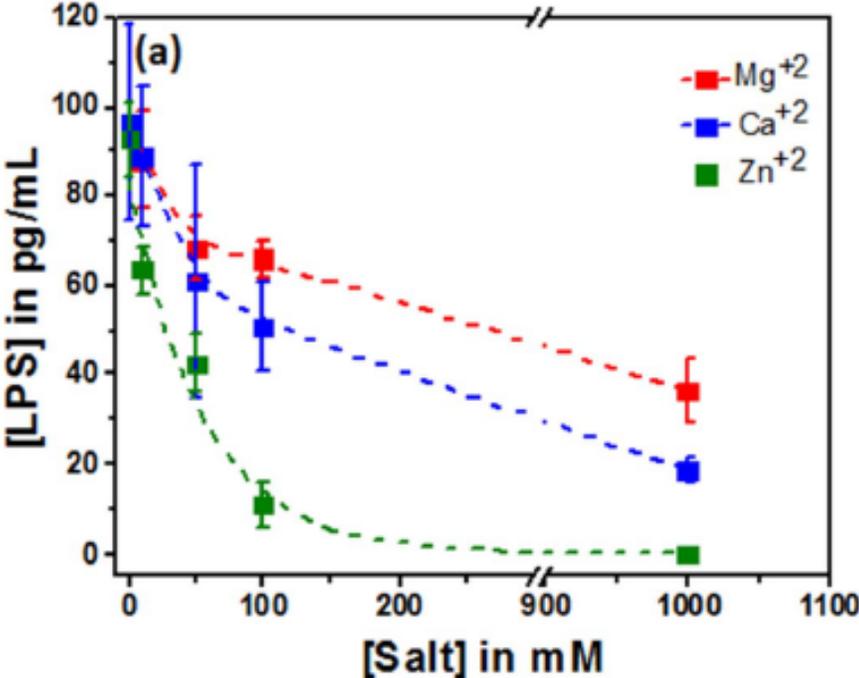


LC droplets - a sensitivity of 0.1-1 pg/mL within one minute, which is more sensitive and faster than commercial LAL assays

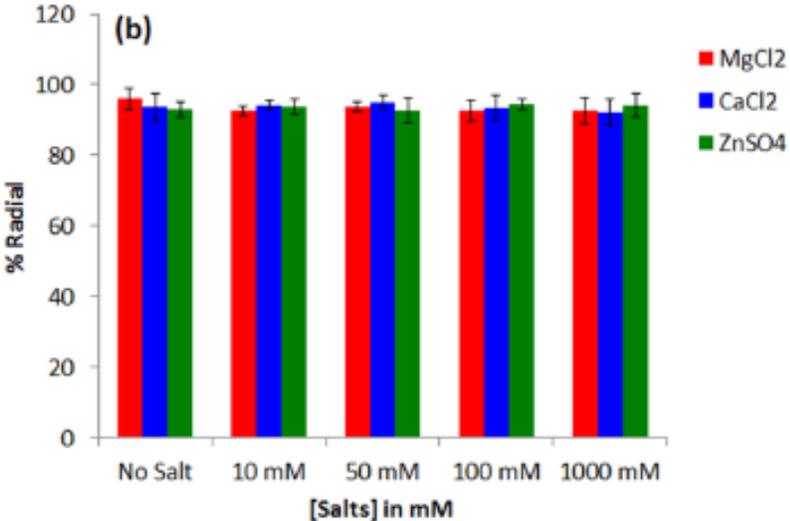
Lin, Miller, Bertics, Murphy, de Pablo, Abbott, *Science* (2011)

# LC Assay Shown to Work in the Presence of Masking Agents

Divalent cations, an example of a masking agent, has been shown **not to interfere** with the liquid crystal assay.



LAL Assay



LCD Assay

# Competition – All Susceptible to LER

THEM

Test	Prevalence	Pros	Cons
Limulus Amebocyte Lysate (LAL) Assay	<ul style="list-style-type: none"> <li>Widely used</li> <li>Offered by CROs and CMOs (Lonza, Charles River, etc.)</li> <li>Kits also available</li> </ul>	<ul style="list-style-type: none"> <li>Understood</li> <li>In use</li> </ul>	<ul style="list-style-type: none"> <li>Inconsistencies batch to batch</li> <li><b>Susceptible to LER</b></li> <li>Matrix effects</li> <li>Uses horseshoe crab blood</li> </ul>
Recombinant Factor C (rFC) Assay	<ul style="list-style-type: none"> <li>Limited offering</li> </ul>	<ul style="list-style-type: none"> <li>Does not use horseshoe crab blood</li> <li>Batch to batch consistency</li> </ul>	<ul style="list-style-type: none"> <li><b>Susceptible to LER</b></li> <li>Uses same coagulation cascade as LAL Assay</li> </ul>
ELISA Assay	<ul style="list-style-type: none"> <li>Limited offering</li> </ul>	<ul style="list-style-type: none"> <li>Does not use horseshoe crab blood</li> </ul>	<ul style="list-style-type: none"> <li><b>Susceptible to LER</b></li> </ul>

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Test	Prevalence	Pros	Cons
<b>LC Assay</b>	<ul style="list-style-type: none"> <li>Ready for partnership</li> </ul>	<ul style="list-style-type: none"> <li>Does not use horseshoe crab blood</li> <li>Batch to batch consistency</li> <li><b>Not susceptible to LER</b></li> </ul>	<ul style="list-style-type: none"> <li>Very early stage</li> </ul>

# Market

- The global endotoxin testing market was valued at \$531.0 million in 2017 and is expected to grow at a CAGR of 18.7%, to reach \$1.3 billion in 2022.

(BCC Research, “Biologics Development and Manufacturing Testing: Technologies and Global Markets” Mar 2018)

- Biopharmaceuticals are a rapidly growing segment of human therapeutics market.
- The surfactants and buffers that are related to LER are increasingly used in parenteral drugs.

## **P09241 – Analyte Detection Using Liquid**

- Three issued US patents (9,080,973; 9,341,570; and 9,547,018)
- One issued patent in China
- One pending application in European Patent Office
- Broad claims to systems and methods of detection
- Priority date April 2009

## **P160072 – Using Liquid Crystal to Detect Endotoxin in the Presence of One or More Potential Masking Agents**

- One pending application in US
- Broad claims to systems and methods of detections in the presence of masking agents
- Priority date December 2015

## Nicholas L. Abbott

- Currently Tisch University Professor at Cornell University
- Previous professor at University of Wisconsin – Madison, and University of California - Davis
- Founder of Platypus Technologies
- Under sponsored research, collaborated with a major pharmaceutical company about solutions for low endotoxin recovery in biologics manufacturing



# Publications

Carter, et al., (2015) “Synthetic Mimics of Bacterial Lipid A Trigger Optical Transitions in Liquid Crystal Microdroplets at Ultralow Picogram-per-Milliliter Concentrations” *Langmuir*, Vol. 31, Issue 47, 12 November 2015, p. 12850-12855

Miller, et al., (2013), “Influence of droplet size, pH and ionic strength on endotoxin-triggered ordering transitions in liquid crystalline droplets”, *Soft Matter*, Vol. 9, Issue 2, 14 January 2013, Pages 374-382

Lin, et al., (2011) Endotoxin-induced structural transformations in liquid crystalline droplets” *Science*, Vol. 332, Issue 6035, 10 June 2011, Pages 1297-1300

# List of Benefits

- ① Biophysical test is more robust and not subject to lot-to-lot variations, requiring constant recalibration.
- ② Not dependent on the coagulation cascade.
- ③ Matrix effects result in inhibition for the standard limulus amoebocyte lysate (LAL) assay.



# Summary

- A new biophysical test has been developed for the detection of endotoxins, and has been proven to out-perform the LAL assay in low endotoxin recovery conditions.
- Proof-of-Concept showed favorable performance versus standard assays.

**Seeking a commercial partner to develop,  
test and launch product.**

- Contact Information:

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# Thank You

