Implementation of rFC: cost considerations

PATH Workshop: Sustainable endotoxin testing: Developing a roadmap for LMIC implementation - Part 2

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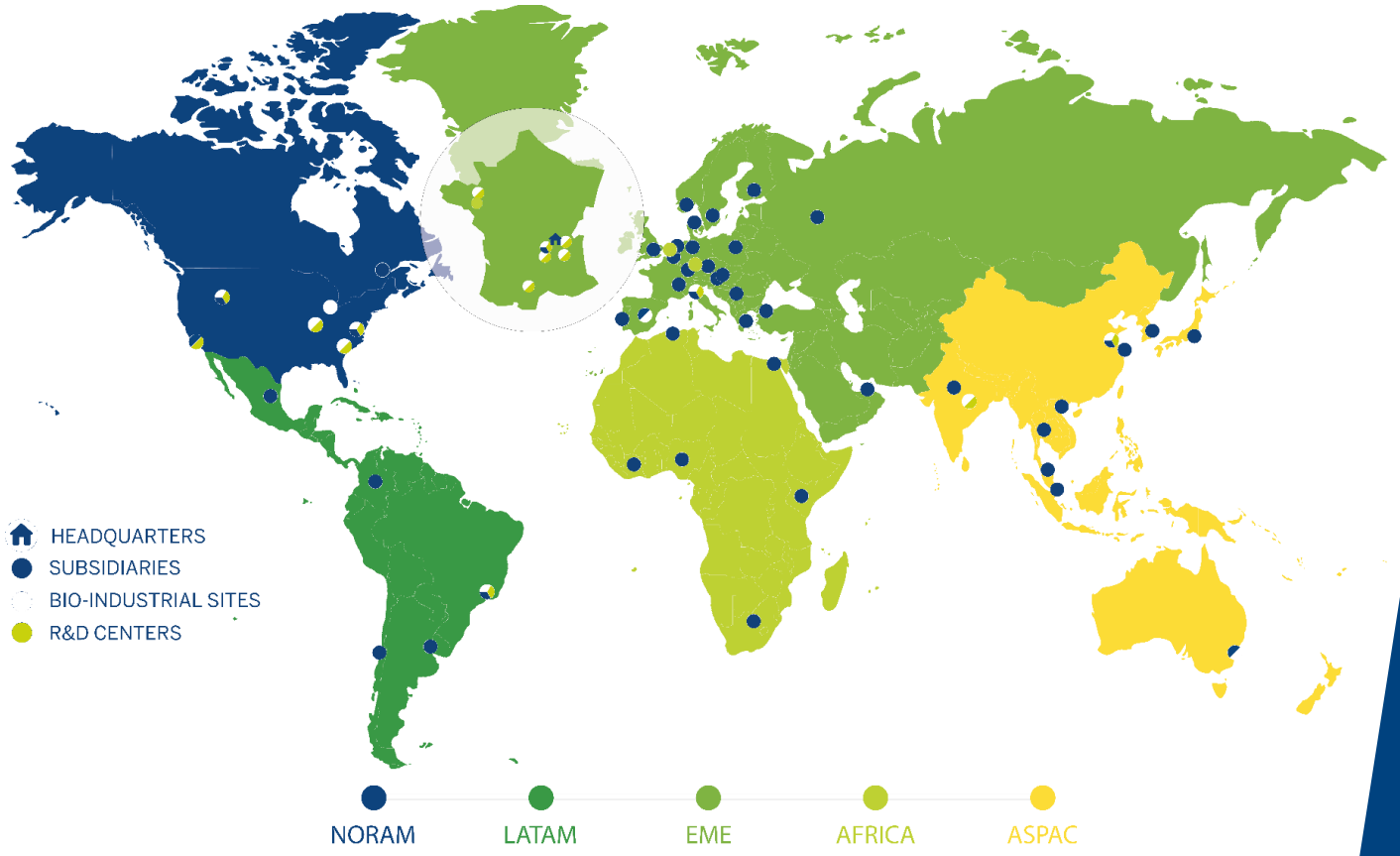
KEY FIGURES



WE ARE LOCATED IN 45 COUNTRIES

and serve more than 160 countries through
a large distribution network

€3.7 billion
in sales in 2023
Organic growth* **+6.6%**

More than **93%**
INTERNATIONAL SALES
(outside of France)

≈14,000
team members worldwide

INNOVATION

12,5% of sales
14 R&D centers
1,900 team members

BIOMÉRIEUX

** Year-over-year, at constant exchange rates and scope.*

ENDONEXT™ : THE COMPLETE rFC SOLUTION

- **Instrument**
  - Agilent SYNERGY HTX Fluorescence/Absorbance plate reader
- **Software**
  - Gen5Secure™
  - ENDONEXT™ V3
- **Reagents**
  - ENDOZYME ® II
  - ENDOZYME ® II GO
  - ENDOZYME ® II GO STRIPS
  - ENDOLISA ®
  - ENDO-RS ®
- **Documents & Services**
  - IOQ Protocols & Execution
  - PQ / MV Protocols
  - Customer Training & Support
  - Feasibility Studies
  - LER / Endotoxin Demasking

METHOD IMPLEMENTATION STEPS

Laboratory Setup & Preparatory Testing

Day 1

Vendor & Local IT

IQ + OQ Synergy HTX Fluorescence Reader & Software

Day 2

3 rFC reagent lots & 2 operators

3 plates

Gain Adjustment

3 plates

Assurance of Criteria for the Standard Curve

1 plate

Temperature Uniformity Test

Method Validation

Required if no compendial chapter available

Day 2 - 3

3 rFC reagent lots & 2 operators & 2 days

Accuracy

Specificity

Precision

Limit of Detection (LOD)

Limit of Quantitation (LOQ)

Linearity

Range

endotoxin-free water

6 plates

Method Suitability

Day 4

1 rFC reagent lot & 3 product lots & 1 operator

1 plate

Non-Interfering Concentration

1 plate

Test for Interfering Factors

Results

Accuracy, Precision & Specificity

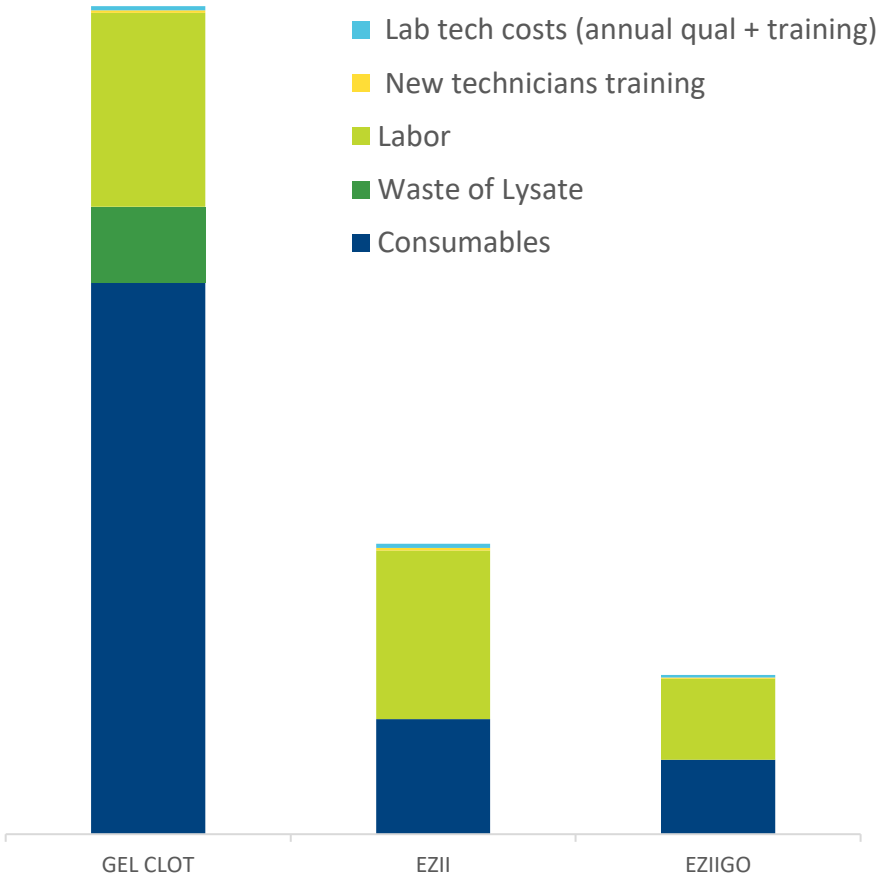
PPC Recovery %:	50-200%
CV% (STD Curve):	<25%
CV% (PPC):	<25%

COST OF IMPLEMENTATION

- Equipment
- Reagents
- Consumables
- Waste of lysate
- Labor
- Training and qualifications

Which of these drivers has the largest impact in your current BET workflow?

COST CALCULATOR CASE: GEL CLOT VS RFC



\+ Investment for testing (instrument, reagents)

\- Consumable cost decrease

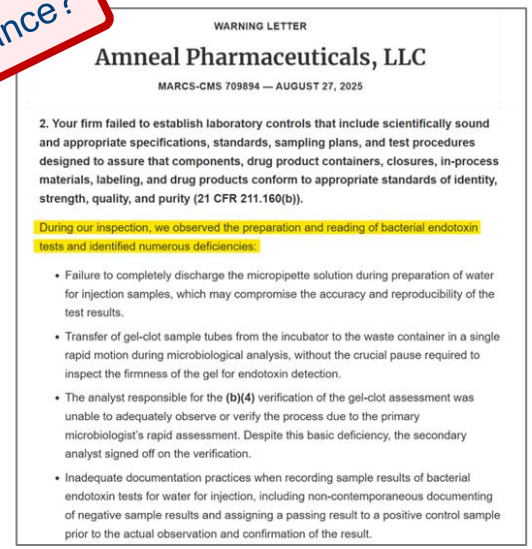
\- Reagent waste decrease

Quantitative results

Improved data integrity

Possible automation

Cost of noncompliance?



WARNING LETTER

Amneal Pharmaceuticals, LLC

MARCS-CMS 709894 — AUGUST 27, 2025

2. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity (21 CFR 211.160(b)).

During our inspection, we observed the preparation and reading of bacterial endotoxin tests and identified numerous deficiencies:

- Failure to completely discharge the micropipette solution during preparation of water for injection samples, which may compromise the accuracy and reproducibility of the test results.
- Transfer of gel-clot sample tubes from the incubator to the waste container in a single rapid motion during microbiological analysis, without the crucial pause required to inspect the firmness of the gel for endotoxin detection.
- The analyst responsible for the **(b)(4)** verification of the gel-clot assessment was unable to adequately observe or verify the process due to the primary microbiologist's rapid assessment. Despite this basic deficiency, the secondary analyst signed off on the verification.
- Inadequate documentation practices when recording sample results of bacterial endotoxin tests for water for injection, including non-contemporaneous documenting of negative sample results and assigning a passing result to a positive control sample prior to the actual observation and confirmation of the result.

HOW CAN BIOMÉRIEUX HELP?

Full setup of the lab

User training

Regulatory Guidance

Execution of PQ (Method Validation)

Support with Method Suitability

Product Feasibility Testing