

---

CENTER FOR DRUG EVALUATION AND RESEARCH

# Guidance for Industry

*The FDA published Good Guidance Practices in February 1997.  
This guidance was developed and issued prior to that date.*

Additional copies are available from:  
Office of Training and Communications  
Division of Communications Management  
Drug Information Branch, HFD-210  
5600 Fishers Lane  
Rockville, MD 20857

(Tel) 301-827-4573  
(Internet) <http://www.fda.gov/cder/guidance/index.htm>

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, FOOD AND DRUG ADMINISTRATION

---



**GUIDELINE ON  
VALIDATION OF THE LIMULUS AMEBOCYTE LYSATE TEST  
AS AN END-PRODUCT ENDOTOXIN TEST FOR HUMAN  
AND ANIMAL PARENTERAL DRUGS, BIOLOGICAL PRODUCTS, AND  
MEDICAL DEVICES**

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION

GUIDELINE ON  
VALIDATION OF THE LIMULUS AMEBOCYTE LYSATE TEST  
AS AN END-PRODUCT ENDOTOXIN TEST FOR HUMAN  
AND ANIMAL PARENTERAL DRUGS, BIOLOGICAL PRODUCTS, AND  
MEDICAL DEVICES

December 1987

Prepared by: Center for Drug Evaluation and Research  
Center for Biologic Evaluation and Research  
Center for Devices and Radiological Health  
Center for Veterinary Medicine

Maintained by: Division of Manufacturing and Product Quality (HFN-320)  
Office of Compliance  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

CONTENTS

INTRODUCTION

I. Background.....1

II. Legal Effect.....3

III. Regulatory Requirements.....4

IV. Human and Animal Drugs and Biological Products.....6

    A. Validation of the LAL Test.....6

    B. Testing of Drugs by the LAL Test.....8

V. Medical Devices.....11

    A. Validation of the LAL Test.....11

    B. Testing of Devices by the LAL Test.....14

VI. Appendices.....16

    A. Initial Quality Control.....17

    B. USP XXI/NF XIV Bacterial Endotoxins Test.....18

    C. Determination of the Relationship Between the Control  
        Standard Endotoxin and the Reference Standard Endotoxin.....19

    D. Maximum Valid Dilution Calculation.....22

    E. Maximum Dose and Endotoxin Limit Table.....25

## INTRODUCTION

This guideline sets forth acceptable conditions for use of the Limulus Amebocyte Lysate test. It also describes procedures for using this methodology as an end-product endotoxin test for human injectable drugs (including biological products), animal injectable drugs, and medical devices. The procedures may be used in lieu of the rabbit pyrogen test.

For the purpose of this guideline, the terms "lysate" or "lysate reagent" refer only to Limulus Amebocyte Lysate licensed by the Center for Biologic Evaluation and Research. The term "official test" means that a test is referenced in a United States Pharmacopeia drug monograph, a New Drug Application, New Animal Drug Application or a Biological License.

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.