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# Contract Test Service

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## Introduction

Associates of Cape Cod,® Inc. Contract Test Service (CTS) laboratory was established over 25 years ago to specialize in testing for endotoxin and glucan contamination and has the most extensive experience of any endotoxin testing laboratory in the world. CTS performs all methods of the LAL assay: gel-clot, chromogenic, and turbidimetric.

The *Limulus* Amebocyte Lysate (LAL) test is a method for the detection and quantitation of bacterial endotoxins. LAL reagents are primarily used to test for endotoxins in injectable pharmaceuticals, biological products, and medical devices. They are also used in renal dialysis centers and a wide range of other applications. LAL tests are described in the Bacterial Endotoxins Test chapter in the United States Pharmacopeia (Chapter <85>) and in the equivalent chapters in the European Pharmacopoeia (Chapter 2.6.14) and the Japanese Pharmacopoeia (General Tests, No. 4.01).

CTS is GMP compliant, ISO registered and licensed by the DEA as a laboratory capable of handling all controlled drug substances except those included in Schedule I. Endotoxin testing can be performed in accordance with FDA, USP, EP and/or JP, depending on the specifications of the client.

In addition to routine testing, CTS has extensive expertise and the ability to:

- Customize endotoxin testing to individual client needs
- Troubleshoot difficult samples
- Develop and/or transfer LAL test methods
- Design and produce custom depyrogenation controls for oven validations

Examples of samples that CTS has experience with:

- Pharmaceutical Drugs, including Class II controlled substances, compounded pharmaceuticals and anti-cancer drugs
- Medical Devices
- Dialysate
- Water
- Air Quality Samples
- Filters
- Veterinary Products
- Cosmetics
- Food Products
- Vaccines

- Tobacco Products
- Machine Oils
- Raw Materials

CTS offers fast processing for routine samples, accurate and reliable test results along with full confidentiality. After sample test results are reviewed, a written report is sent to the client. The client also receives an electronic copy of the report as a pdf if requested.

### CTS Qualifications

- GMP Compliant Laboratory
- FDA Inspected
- DEA Licensed

### Test Methods

- **Gel-clot** - The original LAL assay and the method of reference in most reference manuals (maximum sensitivity 0.03 EU/mL)
- **Turbidimetric** - The most sensitive endotoxin test available in the industry (maximum sensitivity 0.001 EU/mL)
- **Chromogenic** - Color formation is used to quantitate endotoxin (maximum sensitivity 0.005 EU/mL) and glucans

### Test Types

- **Characterization Test** - This test is used to quantify the amount of endotoxin or glucan present in a test sample. A series of dilutions are made in order to find a valid testing dilution which can be used to calculate the endotoxin or glucan concentration of a sample.
- **Validation (USP/EP test for interfering factors)** - This test is used to demonstrate that the product does not interfere with the LAL assay. This test is performed at a dilution that is at or below the Maximum Valid Dilution (MVD) for that product. The MVD is determined by the endotoxin limit for the product. Validation is required for all finished products that are parenteral or intrathecal. The test method should be validated using three lots of the finished product before the Release Test is used to release product. The procedure is also used to demonstrate that the assay is valid when used to test raw or in-process materials.
- **Release Test** - This test is used to release finished products once the assay has been validated. The test is run at the same dilution used in the Validation. The Release Test is also used to release raw materials, in-process materials, and other non-finished goods.

## Drug & Medical Device Testing

### Product Testing

Testing for endotoxin is performed at many steps in the manufacture of drugs and medical devices. Endotoxin testing is required for the release of finished product (see Validation of End Product and Release Testing below). Testing for endotoxins is also frequently performed to assess raw materials, in-process materials, vendors, as well as projects and components in research and development. Endotoxin testing is often a component of investigations into product quality issues.

CTS works with clients to perform testing rapidly and assists customer quality departments in identifying endotoxin sources, and troubleshooting product and production issues. CTS can help with integrating endotoxin testing into the quality system at the client's facility.

### Raw Materials Testing

Raw materials can be tested as part of a traditional QC program or Process Analytical Technology (PAT). Identifying the amount of endotoxin in raw materials helps highlight process modifications that can improve the final product. Matching results from raw materials and final product can yield the contribution of each raw material to the endotoxin content of the final product and document improvements in quality during production. Some raw materials should have endotoxin limits established and confirmed to determine if a batch can be accepted from a vendor.

### Validation of End-Product Tests

Three production lots of the final product should be subject to validation (test for interfering factors) before the test may be used to release final product. The validation assay is also used in QC programs to accept raw materials into production. Validation testing can be performed in accordance with USP, EP, and/or JP, depending on the specifications of the client.

### Release Testing

The Release Test is performed according to a validated method and is used to release finished product. The test can also be performed for release of raw/in-process materials. Release testing can be performed in accordance with USP, EP, and/or JP, depending on the specifications of the client.

### Sending Samples

A Sample Submission form must be completed and accompany each sample sent for testing. Sample Submission forms can be obtained from our website at [www.acciusa.com/cts](http://www.acciusa.com/cts) or by calling CTS at (888) 232-5889.

## Custom Services

CTS offers a variety of services that are customized to meet each client's individual requirements.

### Method Development

Some samples or devices interfere with LAL tests and a method must be developed in order to be able to perform a valid test for endotoxin. CTS will determine how best to prepare the sample for testing. We can also perform testing to validate any sample, pre-treatment, and the test method.

### Method Transfer

Many companies have sufficient testing volume to justify performing the assay in-house. For these customers, Associates of Cape Cod, Inc. supplies a complete line of the highest quality LAL reagents. CTS supports this line by working with companies to develop and optimize methods to test products. CTS also helps customers convert from one methodology to another, e.g., from testing by the gel-clot method to chromogenic or turbidimetric assays. The methods developed by CTS are then transferred to the client for use by their own QC laboratories. Your company gets the assurance that the method will work well with your products.

### Custom Depyrogenation Controls

CTS will make custom depyrogenation controls using the same items normally processed in your oven and provide a Certificate of Analysis for the articles. The controls are then used to demonstrate at least a three-log reduction by your oven cycle. CTS can also test items post-depyrogenation to verify oven cycle performance.



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## Contact Information

### U.S. Office

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### Hours of Operation

Monday through Friday, 8:00 a.m. to 5:00 p.m. EST

### U.K. Branch Office

Our UK office also operates a Contract Test Service laboratory for endotoxin and glucan testing. For information on services provided and laboratory qualifications please contact the UK office directly at (44) 151-547-7444 or by email at [info@acciuk.co.uk](mailto:info@acciuk.co.uk)

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## Services Offered

### Characterization Test

#### Gel Clot Method

**GSAM** ----- Initial Test (a series of dilutions)

**GSAM-R** ----- Rush test-48 hour study initiation

**GSAM-S** ----- STAT test-24 hour study initiation

**ESGEL** ----- Endotoxin-specific gel test

**ESGEL-R** ----- Rush test-48 hour study initiation

**ESGEL-S** ----- STAT test-24 hour study initiation

**GREP** ----- Repeat tests, as needed

**GREP-R** ----- Rush test-48 hour study initiation

**GREP-S** ----- STAT test-24 hour study initiation

#### Turbidimetric Method

**TSAM** ----- Initial Test (a series of dilutions)

**TSAM-R** ----- Rush test-48 hour study initiation

**TSAM-S** ----- STAT test-24 hour study initiation

**ESTURB** ----- Endotoxin-specific turbidimetric test

**ESTURB-R** ----- Rush test-48 hour study initiation

**ESTURB-S** ----- STAT test-24 hour study initiation

**TREP** ----- Repeat tests, as needed

**TREP-R** ----- Rush test-48 hour study initiation

**TREP-S** ----- STAT test-24 hour study initiation

#### Chromogenic Method

**CSAM** ----- Initial Test (a series of dilutions)

**CSAM-R** ----- Rush test-48 hour study initiation

**CSAM-S** ----- STAT test-24 hour study initiation

**ESCHRM** ----- Endotoxin-specific chromogenic test

**ESCHRM-R** ----- Rush test-48 hour study initiation

**ESCHRM-S** ----- STAT test-24 hour study initiation

**CREP** ----- Repeat tests, as needed

**CREP-R** ----- Rush test-48 hour study initiation

**CREP-S** ----- STAT test-24 hour study initiation

**ESAM** ----- Endospey® test (research use only)

**ESAM-R** ----- Rush test-48 hour study initiation

**ESAM-S** ----- STAT test-24 hour study initiation  
**GLUC** ----- GlucateLL® (1→3)-β-D-glucan specific test (research use only)  
**GLUC-R** ----- Rush test-48 hour study initiation  
**GLUC-S** ----- STAT test-24 hour study initiation  
**GLUR** ----- GlucateLL® re-tests, as needed  
**GLUR-R** ----- Rush test-48 hour study initiation  
**GLUR-S** ----- STAT test-24 hour study initiation

**Validation (USP/EP test for interfering factors)**

*Characterization of samples must be done prior to validation testing*

**GVAL** ----- Gel-clot method  
**GVAL-R** ----- Rush test-48 hour study initiation  
**GVAL-S** ----- STAT test-24 hour study initiation  
**TVAL** ----- Turbidimetric method  
**TVAL-R** ----- Rush test-48 hour study initiation  
**TVAL-S** ----- STAT test-24 hour study initiation  
**CVAL** ----- Chromogenic method  
**CVAL-R** ----- Rush test-48 hour study initiation  
**CVAL-S** ----- STAT test-24 hour study initiation  
**EGVAL** ----- Endotoxin-specific gel-clot method  
**EGVAL-R** ----- Rush test-48 hour study initiation  
**EGVAL-S** ----- STAT test-24 hour study initiation  
**ETVAL** ----- Endotoxin-specific turbidimetric method  
**ETVAL-R** ----- Rush test-48 hour study initiation  
**ETVAL-S** ----- STAT test-24 hour study initiation  
**ECVAL** ----- Endotoxin-specific chromogenic method  
**ECVAL-R** ----- Rush test-48 hour study initiation  
**ECVAL-S** ----- STAT test-24 hour study initiation

**Release Testing**

**GREL** ----- Gel-clot method  
**GREL-R** ----- Rush test - 48 hour study initiation

**GREL-S** ----- STAT test - 24 hour study initiation  
**TREL** ----- Turbidimetric method  
**TREL-R** ----- Rush test - 48 hour study initiation  
**TREL-S** ----- STAT test - 24 hour study initiation  
**CREL** ----- Chromogenic method  
**CREL-R** ----- Rush test - 48 hour study initiation  
**CREL-S** ----- STAT test - 24 hour study initiation  
**EGREL** ----- Endotoxin-specific gel-clot method  
**EGREL-R** ----- Rush test - 48 hour study initiation  
**EGREL-S** ----- STAT test - 24 hour study initiation  
**ETREL** ----- Endotoxin-specific turbidimetric method  
**ETREL-R** ----- Rush test - 48 hour study initiation  
**ETREL-S** ----- STAT test - 24 hour study initiation  
**ECREL** ----- Endotoxin-specific chromogenic method  
**ECREL-R** ----- Rush test - 48 hour study initiation  
**ECREL-S** ----- STAT test - 24 hour study initiation

**Custom Services**

**COVN** ----- Oven depyrogenation validation  
**CMTN** ----- Methods transfer (in-lab technician training)  
**CTQN** ----- Technician qualification (in-lab, one-on-one training)  
**CSOP** ----- SOP writing of developed method

**Additional Services**

**RTRND** ----- Special shipping (samples sent to alternate location)  
**CSET** ----- One-time new customer set-up fee

**Labor**

**PREP** ----- Additional sample prep/ extraction/unusual treatment or handling  
**PREP-R** ----- Rush test - 48 hour study initiation  
**PREP-S** ----- STAT test - 24 hour study initiation



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