Enabling a Healthier World

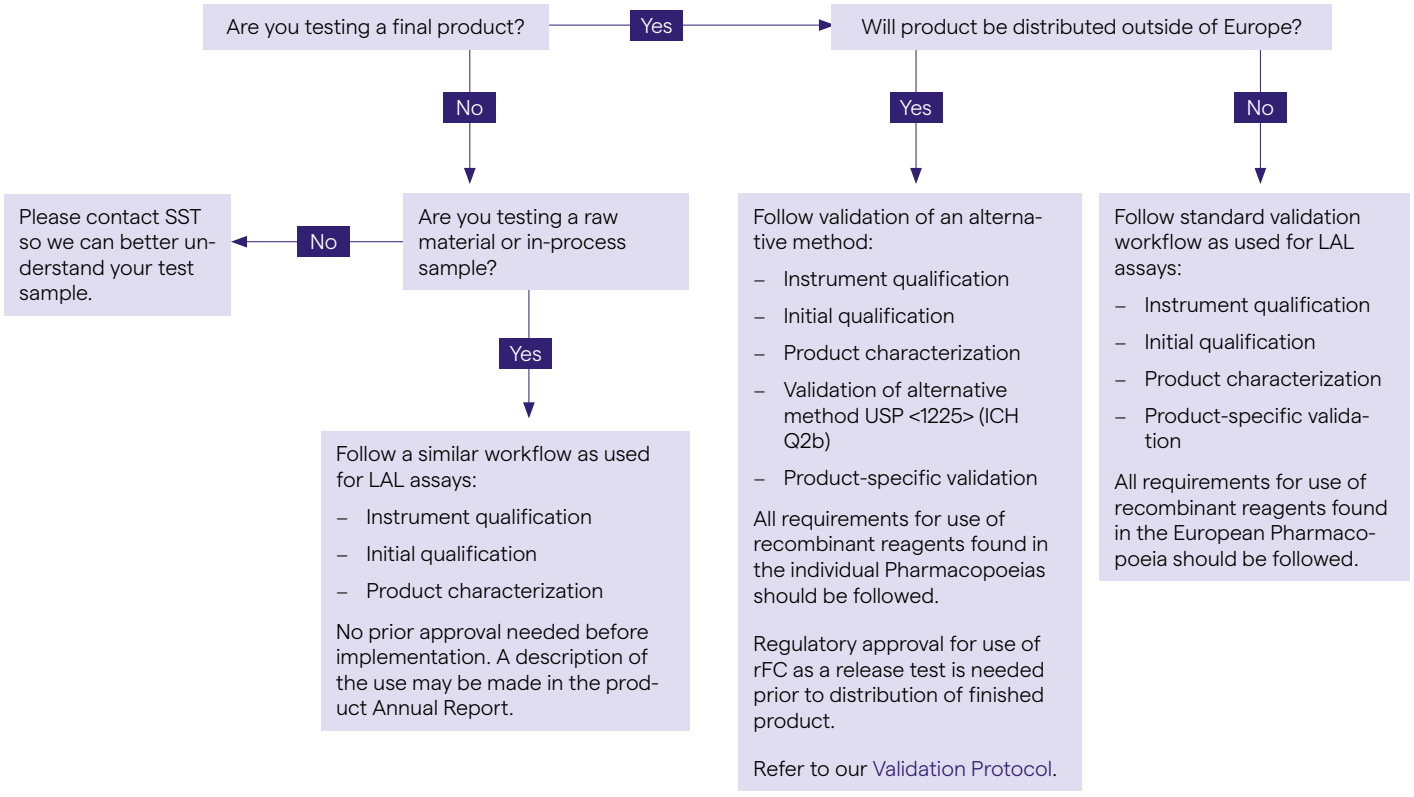
Lonza

PyroGene® rFC Assay Validation Considerations

Since its introduction in 2003, Lonza's PyroGene® Recombinant Factor C Assay has grown in use and acceptance with industry users and regulators. Today, this assay is used worldwide across many pharmaceutical industry segments.

The rFC assay can be used to test for the presence of endotoxin in raw materials, in-process samples and final product and implementing the assay is easier than commonly anticipated. This decision tree can help clarify the requirements so you can reap the immediate benefits of using Lonza's recombinant technology.

Decision Tree



Description of Validation Steps

Instrument Qualification

This step is performed when new equipment is installed and involves Installation Qualification (IQ), Operational Qualification (OQ), Performance Qualification (PQ) activities. If equipment is already in place and qualified, this step can be skipped.

Initial Qualification

This test is designed to validate that the LAL/rFC test system, including analysts, reagents and equipment, are working properly. This test should be conducted each time the laboratory receives a new batch/lot of reagents.

Product Characterization

Product Characterization (also known as Inhibition/Enhancement Testing) will determine the optimal conditions for the product being tested. A majority of the products tested for endotoxin interfere with the assay to some degree. It is often possible to overcome interference by diluting the sample with Water for Bacterial Endotoxins Test (BET) to a point at which the interfering factor ceases to affect the test, but the endotoxin limit concentration is still detectable. This is the simplest and most widely used technique for overcoming interference and should be tried before other methods of addressing interference.

Validation of Alternative Method

The purpose of this step is to show that the rFC assay is equivalent to other photometric endotoxin test methods that use LAL to detect endotoxins. This involves generating data for assay parameters listed in USP <1225> (ICH Q2b). These parameters include specificity, precision, accuracy, linearity, detection limit, quantification limit, range and robustness. The procedure to follow is included in our Validation Protocol.

Product-specific Validation

For product validation, typically 3 lots of product are tested at the optimal conditions determined during product characterization to show repeatability. Good quality practices should include samples that represent the batch.

PyroGene® rFC Assay Validation Timeline

One validation can be accomplished in as little as 5 days assuming that the product has been previously validated with a quantitative LAL method.

Product Validation of PyroGene® rFC Assay at a Glance

2 days	0.5 days	>0.5 days (min.)	>1.5 days (min.)	0.5 days
Preparation	**Initial qualification**	**Inhibition/ enhancement testing**	**Validation of alternative method**	**Product validation**
• IOP/Q • Sensitivity assay for rFC • Initial qualification of current and rFC method and analyst	• Not necessary if previously qualified reagent lots are used	• Only for rFC • Time depending on extent of testing required to find a suitable dilution/pre-treatment	• Tests with both current and rFC method • Good planning can save time	• 3 production lots

*We offer a full Validation Protocol that can be followed for your convenience.
For further information, please submit your Validation Protocol Request or contact our Scientific Support Team.

Resources

1. U.S Department of Health and Human Services, Food and Drug Administration, Guidance for Industry Pyrogen and Endotoxins Testing: Questions and Answers (June 2012). https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-pyrogen-and-endotoxins-testing-questions-and-answers
2. European Directorate for the Quality of Medicines (EDQM). European Pharmacopeia chapter 2.6.32: Test for bacterial endotoxins using recombinant factor C, Edition 11.
3. Product Validation Protocol for the Lonza PyroGene® rFC Endotoxin Detection Assay. https://bioscience.lonza.com/lonza_bs/GB/en/pyrogene-validation-request-form
4. Preparing for the Future of QC Testing: Straightforward Adoption of Sustainable Endotoxin and Pyrogen Tests. White Paper. www.lonza.com/qcinsider

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Learn more.

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