charles river

BIOLOGICS TESTING SOLUTIONS

Pyrogenicity, Endotoxin and Monocyte Activation Testing

Assays Offered

- *In vivo* pyrogenicity testing
- *In vitro* bacterial endotoxin testing
- Monocyte activation testing (MAT)

Pyrogen and endotoxin detection is offered as part of our process manufacturing support network and lot release testing services as a vital step before a product is released to the market. Charles River offers a number of testing methods to best suit the unique pyrogen and endotoxin needs of our clients' products.

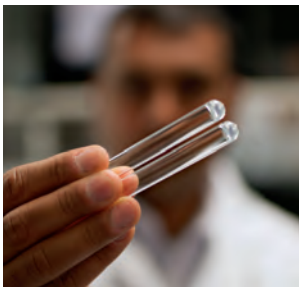
Pyrogenicity Testing

For more than 30 years, Charles River has conducted *in vivo* pyrogen testing with speed and accuracy, offering rapid sample turnaround and technical expertise. We perform this critical component of our clients' quality control program in our dedicated Good Manufacturing Practice (GMP)-compliant facilities using our own specific pathogen-free (SPF) rabbits. Test items include protein-based material, non-protein material and blood products. All tests are compliant with both USP <151> and EP 2.6.8 standards.

The rabbit pyrogen test remains a viable mammalian test model to use when testing for non-endotoxin pyrogens and a variety of products for which the LAL method is limited. One-time pyrogen testing may also be required by regulatory authorities to support routine use of endotoxin tests.

Endotoxin Testing

We also offer *in vitro* bacterial endotoxin testing. Assays are performed to meet all of the pharmacopoeia requirements, including gel-clot (qualitative), and turbidimetric kinetic and chromogenic (quantitative) methods. We provide preliminary screening and validation of products as well as a backup technical service to clients.



Services

- *In vitro* and *in vivo* methods
- R&D and GMP applications
- Product-specific validations

Monocyte Activation Testing

Reflecting our strong commitment to the 3Rs, Charles River continuously seeks new methods and technologies to provide clients with viable *in vitro* alternatives to *in vivo* tests. In this accord, we offer the monocyte activation test (MAT) according to EP 2.6.30.

The MAT works by predicting the human response to pyrogens on the basis of human fever, and may be used as an alternative to the rabbit pyrogen test. This assay can be used to detect Gram-positive and Gram-negative organisms and parasitic, viral and other biological pyrogens (e.g., yeast). It also offers a solution for the testing of products that prove problematic in other *in vitro* endotoxin tests, such as drugs that affect body temperature regulation (e.g., antipyretic drugs and steroids), drugs that cause immunological reactions (e.g., immunoglobulins), detergents, some blood-derived products (e.g., stem cells) and other products that are turbidimetric, strongly colored or interfere with clotting.

When required, our scientific staff can work with clients to develop other approaches to the MAT to satisfy testing objectives.

Pyrogen Detection Application Suitability

		Rabbit Pyrogen Test	Endotoxin (LAL)	MAT
		Principle of Test		
		Fever Reaction Mammal	Defense Mechanism Arthropoda	Fever Reaction Human
Detectable Pyrogens	Gram-negative	+	+	+
	Gram-positive	+	–	+
	Fungi	+	–	+
	Virus	+/–[1]	–	+
Applications	Pharmaceuticals	+	+	+
	Biologics	+	+/–[2]	+
	Blood components	–	–	+
	Cellular products	–	+/–	+
	Air pollutants	+[3]	+/–[3]	+
	Medical devices	+[3]	+/–[3]	+

[1] Variable pyrogenic responses
[2] Rabbit testing often required
[3] Can only be tested indirectly by extracting device or filter with pyrogen-free water or saline

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