Press release

16 July 2024, Strasbourg, France

European Pharmacopoeia bids adieu to rabbit pyrogen test in its monographs

In a landmark decision for both animal welfare and scientific advancement, the European Pharmacopoeia Commission (EPC) decided to eliminate the Rabbit Pyrogen Test (RPT) from its monographs during its 179th session in June 2024.

Pyrogens are fever-inducing contaminants that may unintentionally be present in medicines administered by injection (including vaccines, blood products, radiopharmaceuticals, antibiotics and large volume solutions for infusion). Their detection is therefore essential to ensure that medicines administered by this route are safe.

For decades, the RPT has been the traditional method of detection. The RPT involves measuring the rise in body temperature in rabbits following intravenous injection of the test substance. Despite multiple efforts to encourage medicine developers to move away from the RPT, the test is still widely used to detect pyrogens, consuming around 400 000 rabbits /year[1] worldwide.

Following a broad exercise aiming at the complete removal of the RPT from the European Pharmacopoeia (Ph. Eur.), in June 2024 the EPC adopted 57 revised texts from which the RPT has been deleted, together with a new general chapter on *Pyrogenicity (5.1.13)*, marking the end of the RPT era in the Ph. Eur.

This is a major achievement for animal welfare and for the advancement of modern *in vitro* approaches for pyrogenicity testing. As a result, no Ph. Eur. text will require the use of the RPT; instead, it will be up to the medicine developer to select a suitable *in vitro* test (e.g. the monocyte-activation test) to control the pyrogenicity of their product, based on a risk assessment as described in the new general chapter.

In accordance with the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (ETS No. 123), the EPC is committed to the reduction of animal usage wherever possible in pharmacopoeial testing. This historic step is an illustration of this commitment and will have a significant impact on the replacement, reduction and refinement of animal tests in the quality control of medicines.

The revised texts omitting the RPT and the new chapter, *Pyrogenicity (5.1.13)*, will be published in Supplement 11.8 of the Ph. Eur., with an implementation date of 1 July 2025.

Background information

- The European Pharmacopoeia
- The Council of Europe / EDQM and alternatives to animal testing

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Note for the Editor: Further information is available on our website: **www.edqm.eu**.

1. Hartung T. (2015), "The human whole blood pyrogen test – lessons learned in twenty years", ALTEX - *Alternatives to animal experimentation*, 32(2), pp. 79–100. DOI: 10.14573/altex.1503241.

The EDQM is a leading organisation that protects public health by enabling the development, supporting the implementation and monitoring the application of quality standards for safe medicines and their safe use. Its standards are recognised as a scientific benchmark worldwide. The European Pharmacopoeia is legally binding in member states.[2] The EDQM also develops guidance and standards in the areas of blood transfusion, organ transplantation and consumer health issues.

A political organisation set up in 1949, the Council of Europe works to promote democracy and human rights continent-wide. It also develops common responses to social, cultural and legal challenges in its 46 member states.

2. The European Pharmacopoeia Commission comprises 40 members: Albania, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Republic of Moldova, Montenegro, Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Türkiye, Ukraine, United Kingdom and the European Union.