FOI 24/142- Eye Irritation Toxicity Tests

MHRA Customer Services <MHRACustomerServices@mhra.gov.uk>
Wed 28/02/2024 14:42
To [redacted]
FOI 24/142

Dear [redacted]

Regarding your request of 10 February 2024, please see below our responses to your questions.

1. Please explain why commercial companies are still using 'in vivo' tests in these circumstances to test medical products for eye irritation before being sent to human clinical trials
The MHRA is not aware that companies are doing such tests to initiate clinical trials in the UK: although a systematic review is not possible because this would involve too much resource to review every past application for the first UK clinical trial with a new agent, no examples can be recalled in which in vivo eye irritation testing data were presented to support a clinical trial. The MHRA does not ask, expect or require companies to conduct in vivo testing in animals to assess eye irritation.

However, this law requiring use of non-animal alternatives where available, may not be the same in other countries and it may be that companies operating in other countries do such tests to meet expectations of other regulators. If such tests are done, the MHRA's expectation is that this information will be supplied to the MHRA because there is an overarching principle that a company, when it makes an application to the regulatory authority, will submit information on all studies seeking to establish the safety assessment of a new agent.

2. Please explain why commercial companies are still using 'in vivo' tests in these circumstances to batch test already commercially available products for eye irritation and you are issuing them with GLP compliance documents.
The United Kingdom Good Laboratory Practice Monitoring Authority is not responsible for specifying what testing is required to be conducted to Good Laboratory Practice (GLP). Requirements to conduct any type of testing in accordance with GLP would need to be raised with the specific regulatory authority requiring the testing.

If you are dissatisfied with the handling of your request, you have the right to ask for an internal review. Internal review requests should be submitted within two months of the date you receive this response and addressed to: info@mhra.gov.uk

Please remember to quote the reference number above in any future communications.

If you were to remain dissatisfied with the outcome of the internal review, you would have the right to apply directly to the Information Commissioner for a decision. Please bear in mind that the Information Commissioner will not normally review our handling of your request unless you have first contacted us to conduct an internal review. The Information Commissioner can be contacted at:

Information Commissioner's Office
Wycliffe House
Water Lane
Wilmslow
Cheshire
SK9 5AF

Yours sincerely,

MHRA Customer Experience Centre
Communications and engagement team
Medicines and Healthcare products Regulatory Agency
10 South Colonnade, Canary Wharf, London E14 4PU

Dear Medicines and Healthcare Products Regulatory Agency, Eye Irritation toxicity tests.
Quote : Animals(Scientific Procedures)Act 1986, Section 2A.
[F12APrinciples of replacement, reduction and refinement (1)The Secretary of State must exercise his or her functions under this Act with a view to ensuring compliance with the principles of replacement, reduction and refinement.
(2)For the purposes of this Act—
(a)the principle of replacement is the principle that, wherever possible, a scientifically satisfactory method or testing strategy not entailing the use of protected animals MUST be used instead of a regulated procedure; The word MUST is an absolute. No exemptions, no loopholes, no work arounds, no lack of investment or training or skills stopping it.

Here are the validated replacements for the Eye Irritation toxicity Tests Validated Non-Animal Methods
a) Integrated approach on testing and assessment (IATA) for serious eye damage and irritation OECD guidance document (GD) 263, published in 2017
b) Chemical toxicity assessment strategy -- European Chemicals Agency guidance Chapter R.7a., R.7.2.8–R.7.2.11 (2017)
c) Use of a testing framework employing cytosensor microphysiometer (CM), BCOP, and the EpiOcular™ model for classification of pesticide products -- US Environmental Protection Agency policy (2015)
d) Reconstructed human cornea-like epithelium (RhCE) test method EpiOcular™ (MatTek, US) OECD test guideline (TG) 492, revised in 2019 ESAC statement (2014); JaCVAM statements (2017 and 2018); KoCVAM guideline (2016) SkinEthic™ (L'Oréal, France) LabCyte (J-TEC, Japan) MCTT HCE™ (Biosolution Co, Ltd, South Korea)
e) Fluorescein leakage (FL) test method OECD TG 460, revised in 2017 ESAC statement (2009); JaCVAM statement (2013)
f) Short time exposure (STE) in vitro test method OECD TG 491, revised in 2018 ICCVAM report (2013); JaCVAM statement (2016); KoCVAM guideline (2017)
g) Vitrigel-eye irritancy test (EIT) method OECD TG 494, published in 2019
h) In vitro macromolecular test method OECD TG 496, published in 2019
i) Bovine corneal opacity and permeability (BCOP) test method OECD TG 437, revised in 2017 ICCVAM report (2006); ESAC statement (2007); JaCVAM statements (2009 and 2014); KoCVAM guideline (2011)
j) Isolated chicken eye (ICE) test method OECD TG 438, revised in 2018 ICCVAM report (2006); ESAC statement (2007); JaCVAM statement (2009)
k) Cytosensor microphysiometer (CM) assay -- ESAC statement (2009); ICCVAM report (2010)

Reference: PSCI-Alternate-Methods-8.5x11-2021_300.pdf

Please explain why commercial companies are still using 'in vivo' tests in these circumstances:
1. To test medical products for eye irritation before being sent to human clinical trials 2. To batch test already commercially available products for eye irritation and you are issuing them with GLP compliance documents