Medicines & Healthcare products
Regulatory Agency

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[redacted]
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30 May 2024

MHRA reference: **FOI2024/00082**

Dear [redacted],

Thank you for your information request, which we received on **1 May**. You asked for:

> *"The Department of Health and Social Care, confirmed in response to FOI 1500415 that you are regulatory body responsible for the batch testing of products for eye irritation.*
>
> *What advice are you, providing the laboratories providing the batch testing of products for eye irritation given that you subscribe to the 3R's and will know that all eye irritation tests have replaced 'in vivo' tests with 'in vitro'.*
> *Please could you direct me to the guidance you are providing on this matter."*

We have dealt with your request under the Freedom of Information Act 2000 (FOIA).

As mentioned in the conclusion of this letter, MHRA do not provide specific guidance to laboratories testing medical devices for ocular irritation. Therefore, under Section 1(1)(a) of the FOI Act we confirm that this information is not held.

Advice and assistance
To assist you to locate the relevant ISO guidelines on the above link, and to provide relevant/useful context we provide the below.

With regards to medical devices, MHRA do *not* conduct batch testing to determine the potential for eye irritation.

It is the responsibility of the manufacturer to assess the safety of the medical device according to the intended purpose prior to its placement on the market. For a medical device to be placed on the UK market affixed with a CE or UKCA mark, the

manufacturer must demonstrate conformance to the relevant regulations, the EU MDR 2017 or the UK MDR 2002 respectively.

The EU MDR 2017 and the UK MDR 2002 contain specific requirements that relate to the choice of materials and substances used, particularly as regards toxicity and the compatibility between the material and substances used and the biological tissues, cells and body fluids.

Guidance on these requirements is provided by the international series of standards ISO 10993 -Biological evaluation of medical device.

ISO 10993-1:2018 Biological evaluation of medical devices – Evaluation and testing within a risk management process is the umbrella standard which '*aims to protect humans from potential biological risks arising from the use of medical devices. A secondary role is to utilize scientific advances in our understanding of basic mechanisms, to minimize the number and exposure of test animals by giving preference to in vitro models and to chemical, physical, morphological, and topographical characterization testing, in situations where these methods yield equally relevant information to that obtained from in vivo models.'*

The biological evaluation of a medical device is set out within a risk management process and helps to determine if the medical device is free from unacceptable biological risk in context of the intended use. Biological evaluation starts with the categorisation of the medical device according to type and duration of body contact, this facilitates selection of appropriate data sets for evaluation and determines the necessary rigour in the biological evaluation. An assessment of all available information is conducted, including but not limited to physical and chemical characteristics of the material/medical device, clinical data, toxicology or biological safety data and test procedures. This information is compared to the data set(s) needed to assess the biological safety of the medical device. According to ISO 10993-1:2018*, 'testing is usually not necessary when sufficient information is already available to perform a risk assessment of the material and/or the medical device.'*

Where it is deemed necessary by the manufacturer to perform testing, ISO 10993-1:2018 recommends a tiered approach to testing, conducted in the following sequence.

1) Physical and chemical characterization
2) *In vitro* testing
3) Animal testing

ISO 10993-1:2018 states that, '*the final animal testing step should only be carried out if the prior characterization tests and in vitro studies do not provide sufficient information.'* Where animal testing is considered, ISO 10993-2 Biological evaluation of medical devices- Animal welfare requirements applies. *ISO 10993-2 describes animal welfare aspects for performing animal studies for the biological evaluation of*

medical devices thereby also emphasizing the 3R's for replacement, reduction, and refinement of animal studies.

Where irritation testing is deemed necessary by the manufacturer to perform a risk assessment, guidance is provided in the ISO 10993 series of standards. ISO 10993-23:2021 Biological evaluation of medical devices- Tests for irritation assesses possible contact hazards from medical devices which can produce irritation. This document describes validated *in vitro* tests for the detection of irritant chemicals in medical device extracts that can replace the *in vivo* rabbit test for irritation by skin exposure and by intracutaneous administration.

ISO 10993-23:2021 provides guidance on special irritation tests including ocular irritation tests and states that '*the ocular irritation test should only be considered if safety data cannot be obtained by other means, and only for materials that come into contact with the eye or eyelid.' In vitro* alternative tests for ocular irritation are available but are not yet validated for medical device extracts. However, ISO 10993-23:2021 notes that *'strategic combinations of several alternative test methods within a (tiered) testing strategy can be able to replace the Draize eye test.'* The Draize eye test is an *in vivo* ocular irritation test.

The ISO 10993 series contains guidance on testing of medical devices. MHRA do not provide specific guidance to laboratories testing medical devices for ocular irritation.

The step wise approach of ISO 10993-1:2018 is such that animal testing is considered last, only where there is insufficient information available by other means to perform a risk assessment.

References/resources:
Information published by the International Organization for Standardization, European Union, and the British Government .

ISO Guidelines
ISO - Publicly available resources

EU MDR 2017
https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745

UK MDR 2002
The Medical Devices Regulations 2002 (legislation.gov.uk)

This concludes our response to your request.

If you have a query about this response, please contact us at foi.request@mhra.gov.uk.

Medicines & Healthcare products Regulatory Agency

Please remember to quote the reference number at the top of this letter in any future communications. Details of your appeal rights are below.

Yours sincerely,

Healthcare, Quality and Access Group

Medicines and Healthcare products Regulatory Agency

Appeal rights

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

If you remain dissatisfied with the outcome of the internal review, you 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 a request unless the requester has first asked us to conduct an internal review.

The Information Commissioner can be contacted through their online webform at: https://ico.org.uk/make-a-complaint/foi-and-eir-complaints/foi-and-eir-complaints/

Or in writing to: Information Commissioner's Office, Wycliffe House, Water Lane, Wilmslow, Cheshire, SK9 5AF

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