
OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

CONSIDERATIONS FOR OPHTHALMIC PRODUCTS

I. Purpose 1
II. Ophthalmic Review Considerations 1
III. References 2
IV. Version history..... 2

I. Purpose

In a statement of policy issued on September 1, 1964, the Food and Drug Administration ruled that liquid preparations offered or intended for ophthalmic use that are not sterile may be regarded as adulterated within the meaning of 501(c) of the Federal, Food, Drug, and Cosmetic Act (the FD&C Act), and further, may be deemed misbranded within the meaning of section 502(j) of the FD&C Act. On October 28, 1972, this ruling extended to all preparations for ophthalmic use.

The purpose of this policy and procedure manual is to provide reviewers with some guidance for the evaluation of ophthalmic products.

II. Ophthalmic Review Considerations

It is the policy of the Center that, as presently stated, 21 CFR 200.50 pertains to all animal ophthalmics including aerosols and powders. This information should be communicated to sponsors during discussions or pre-submission conferences. For Division of Manufacturing Technologies (DMT) reviewers, this policy means that manufacturers should use a process that yields an ophthalmic product with appropriate sterility assurance and that sterility testing or a suitable mitigation strategy (e.g., parametric release) is essential for all ophthalmic products.

The Center is mindful of the National Academy of Sciences/National Research Council recommendation that use of powders and aerosols in the eyes should not occur, because these dosage forms tend to produce foreign body reactions. Unless the sponsor demonstrates that this is not a risk with their product, the Center discourages development of ophthalmic products delivered as powders/aerosols. Target Animal Division (TAD) reviewers should evaluate applications utilizing these routes of administration on a case-by-case basis and request appropriate target animal safety data for the particular product.

Pyrogens (endotoxins) can be a safety concern depending on the intended use of the ophthalmic product.¹ For intraocular products (e.g., products administered by injection), an endotoxin limit is necessary. For topical ophthalmics, the need for an endotoxin limit will be determined on a case-by-case basis considering the safety risk to the animal (e.g., risks presented to animals with ulcers or open

wounds on the eye surface). Division of Manufacturing Technologies reviewers should discuss the need for endotoxin limits for topical ophthalmics with the appropriate TAD for the product.

III. References

¹Guidance for Industry: Pyrogen and Endotoxins Testing: Questions and Answers

IV. Version history

4/25/00 P&P established

8/25/14 Updated the P&P format to be 508 compliant. The new title reflects more than just sterility for ophthalmics. The new paragraph regarding sterility highlights how the reviewer should be applying the policy. This version modifies the language regarding powders and aerosols and clarifies how the reviewer should be applying the policy. This version also amends the pyrogen/endotoxin paragraph to allow greater flexibility in the application of an endotoxin limit based on the route of administration of the ophthalmic product and clarifies how the reviewer should be applying the policy.