

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Atropine Sulfate

February 2022

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

This is a new draft product-specific guidance for industry on generic atropine sulfate.

Active Ingredient:	Atropine sulfate
Dosage Form; Route:	Solution/drops; ophthalmic
Strength:	1%
Recommended Study:	Request for waiver of in vivo bioequivalence study requirements

Additional Comments: Atropine sulfate (1%) ophthalmic solution products should have comparable physicochemical properties to the Reference Standard (RS) including but not limited to pH, specific gravity, buffer capacity, osmolality, and viscosity, if applicable. Comparative analysis should be performed on three exhibit batches, if available, of both test and RS products.

Waiver:

To qualify for a waiver from submitting an in vivo bioequivalence (BE) study on the basis that BE is self-evident under 21 CFR 320.22(b), a generic atropine sulfate (1%) ophthalmic solution

product must be qualitatively (Q1)¹ and quantitatively (Q2)² the same as the Reference Listed Drug (RLD).

An in vivo BE study is requested for any atropine sulfate (1%) ophthalmic solution product that has a different inactive ingredient from the RLD,³ a difference of more than 5% in the amount of any inactive ingredient compared to that of the RLD, or differences in comparative physicochemical characterization data.

Unique Agency Identifier: PSG_206289

¹ Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the reference product.

² Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within $\pm 5\%$ of those used in the reference product.

³ For ophthalmic drug products, FDA has determined that, as a scientific matter, any qualitative or quantitative deviations from the RLD, even in inactive ingredients listed in 21 CFR 314.94(a)(9)(iv), should be accompanied by an appropriate in vivo BE study or studies. Guidance for industry *ANDA Submissions – Refuse-to-Receive Standards*.