RAAHA LLC

703-587-4864
aloka.srinivasan@gmail.com
www.RAAHALLC.com
3280 Kinross Circle,
Herndon, VA 20171

August 7th, 2024

Via Electronic Submission
Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061, HFA-305
Rockville, MD 20852

CITIZEN PETITION

Raaha LLC. (the "Petitioner") submits this Citizen Petition under the provisions of section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act and 21 CFR § 10.20, 21 CFR § 10.30 and 314.92 requesting that the Commissioner of Food and Drugs refrains from approving an Abbreviated New Drug Application ("ANDA") for Prednisolone Ophthalmic Solution 1% {"Product") without the inclusion of long-term stability studies conducted under refrigerated conditions at 5ºC ± 3 ºC.

A. Action Requested

The Petitioner respectfully requests that the Commissioner of Food and Drugs:

1. Require generic applicants to conduct long-term stability studies that specifically demonstrate the Product's stability over its entire shelf life when stored at refrigerated temperatures (5ºC ± 3 ºC).
2. Refrain from approving any ANDA for a generic version of the Product that does not include data from such long-term stability studies.
3. Revisit the final approval and award of an "AB" rating to ANDA #216935 for the Product, dated June 2, 2024, for applicant Lupin Ltd. ("Lupin") if ANDA #216935 did not include long-term stability studies that specifically demonstrate the Product's stability over its entire shelf life when stored at refrigerated temperatures (5ºC ± 3 ºC), including converting ANDA #216935 approval to a "B" rating until such time as applicant submits such studies.

RAAHA LLC
703-587-4864
aloka.srinivasan@gmail.com
www.RAAHALLC.com
3280 Kinross Circle,
Herndon, VA 20171

B. Statement of Grounds

1. The Reference Listed Drug (RLD) storage statement (attachment 1) implies that product can be stored at:

    - **Controlled room temperature** – per USP<659>: The temperature maintained thermostatically that encompasses the usual and customary working environment of 20º-25ºC (68º-77º F)
    - **Cool temperature** – per USP<659>: Any Temperature between 8º and 15ºC (46º and 59ºF)
    - **Refrigerated** – per USP <659>: A cold place in which the temperature is controlled between 2º and 8º C (36º and 46ºF)

    This storage statement suggests that refrigeration is permitted for storage of the drug product. Therefore, long-term stability studies conducted at 5ºC ± 3ºC should be required in addition to the long-term studies conducted at 25ºC to meet the necessary stability requirements of the product prior to ANDA approval.

    Regarding required Stability studies based on claimed storage conditions, section VIII of the FDA guidance "Quality Considerations for Topical Ophthalmic Drug Products" refers only to a general FDA guidance (FDA guidances for industry Q1A(R2) Stability Testing of New Drug Substances and Products (November 2003); ANDAs: Stability Testing of Drug Substances and Products (June 2013) and ANDAs: Stability Testing of Drug Substances and Products, Questions and Answers (May 2014). Neither of these two guidances adequately addresses the unique stability study conditions associated with Ophthalmic Drug Products that can be refrigerated as per labeled storage condition.

    Additional stability studies are necessary to ensure that any generic version of the Product is stable and effective throughout its shelf life when stored under refrigerated conditions.

    We are concerned that generic versions of the Product may not meet the necessary stability requirements for refrigerated conditions, which could compromise the product's quality, safety and efficacy. The stability of the Product is critical to its performance, and any impact/change in critical quality attributes of the product could lead to adverse events or therapeutic failures.

    We believe that the approval of a generic version of the Product that does not meet the necessary stability requirements for refrigerated conditions could pose a risk to public health. Therefore, we urge the FDA to exercise its authority to ensure that any approved generic version of the Product meets the necessary stability requirements to ensure its safety and efficacy.

703-587-4864
aloka.srinivasan@gmail.com
www.RAAHALLC.com
3280 Kinross Circle,
Herndon, VA 20171

C. Scientific Justification

The Product is a sterile, topical anti-inflammatory agent for ophthalmic use. It is indicated for the treatment of steroid-responsive inflammation of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe.

Ophthalmic suspensions are used to increase the corneal contact time of a drug substance and thus provide a more sustained action. Therefore, the Product is formulated with a water insoluble drug (Prednisolone acetate) in (a micronized form to prevent irritation or scratching of the cornea. The potential for any changes/impact in critical quality attributes of the drug product (like particle size distribution, viscosity, assay of Prednisolone acetate, related substances, re-dispersibility and dissolution) must be evaluated through stability testing during shelf-life at a proposed temperature for storage of the drug product. Specifically, the critical quality attributes like particle size distribution, viscosity and re-dispersibility tend to be impacted by the storage of the drug product at refrigerated conditions. Hence, the stability of the Product is critical to its performance, and any impact/change in critical quality attributes of the product during shelf-life could lead to therapeutic failures or adverse events.

Based on the storage statement provided in the RLD packaging insert (attachment 1), refrigeration is permitted for storage of the drug product and we believe that generic versions of the Product must meet the necessary stability requirements for refrigerated conditions, so as not to compromise the product's quality and further safety and efficacy.

Moreover, storage conditions for pharmaceutical products and materials must comply with their labeling, which is predicated, in part, on the outcomes of stability testing. If stability testing of the product is not performed at the required refrigerated setting, then the labeling could be misleading or inaccurate. Consequently, we assert that the approval of a generic version the Product that does not satisfy the required stability conditions for refrigerated storage could present a significant risk to public health. Therefore, we respectfully urge the FDA to exercise its regulatory authority to ensure that any approved generic version of the Product conforms to the necessary stability study requirements under refrigerated conditions to guarantee its safety and efficacy.

D. Environmental Impact

In accordance with the requirements set forth in 21 CFR § 25.31, Petitioner Raaha LLC hereby requests a Categorical Exclusion from the requirements to prepare an Environmental Impact Assessment.

703-587-4864
aloka.srinivasan@gmail.com
www.RAAHALLC.com
3280 Kinross Circle,
Herndon, VA 20171

E. Economic Impact

Pursuant to 21 CFR §10.30(b) an economic impact analysis will be provided upon request.

F. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to the Petitioner which are unfavorable to the Petition.

Attachments 1- Pred Forte Insert

Please direct any communications regarding this Citizen Petition to Aloka Srinivasan, Ph.D. at telephone +1-703-587-4864 or email: aloka.srinivasan@raahallc.com or (secondary email) alokasrinivasan@gmail.com.

Sincerely,

Aloka Srinivasan

Aloka Srinivasan, Ph.D
Principal and Managing Partner
Raaha LLC
Phone: +1-703-587-4864
Email: aloka.srinivasan@raahallc.com
Email (secondary): alokasrinivasan@gmail.com