Our STN: BL 125473/0
MERCK SHARP & DOHME CORP.
Attention: DR. SCOTT GREENFEDER
P.O. BOX 2000, RY 33-204
RAHWAY, NJ 07065

Dear Dr. Greenfeder:

We are reviewing your biologics license application (BLA) dated January 25, 2013, for "Timothy Grass Pollen Allergen Extract" (GRASTEK) tablet for sublingual use and have determined that the following information is necessary to take complete action. Please promptly submit your written response to the following items so that we may continue evaluating your BLA:

1. The following comments pertain to the (b)(4) steps designated (b)(4)

(b)(4)

2. In section 3.7 of 3.2.S.2.2 DESCRIPTION OF MANUFACTURING PROCESS/PROCESS CONTROLS, you describe an (b)(4). Please provide your study design and data to support this (b)(4)

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3. You indicate tha (b)(4) Tests have been measured for (b)(4) Drug Substance batches. One of the (b)(4) batches failed to meet the acceptance criteria and was rejected (Batch (b)(4)). Please provide the investigation and follow up regarding the reject of Batch (b)(4).

4. It appears that the (b)(4) Test is only performed on the Drug Substance at release. Please clarify if any in-process (b)(4) is performed for the

Drug Substance. If in-process monitoring is not performed please provide a justification and risk assessment for not monitoring (b)(4) during production.

5. Please clarify if a (b)(4) Test is performed on the Drug Substance once it is received from the Catalent Pharma Solutions in Swindon, UK.

6. Concerning the (b)(4) storage containers (b)(4) used for shipment of the Drug Substance.

a. Please clarify whether these containers are single-use or re-used.

b. Are the (b)(4) storage containers (b)(4) received clean, and if so how are they assessed for cleanliness prior to use?

7. Please provide validation data for the (b)(4) assay used to assess integrity of the aluminum blister cards.

8. Please provide data from the lyophilization cycle used for the SCH 697243 Drug Product qualification lots that includes: (b)(4) of lyophilization.

9. Please provide complete OQ and PQ protocols and results for freeze driers (b)(4) freeze driers (b)(4) . Please include any testing and data confirming that all (b) (4) freeze dryers are of similar design and operating principle, and detailed explanation of any deviations which occurred during the validation.

10. Please provide the (b)(4) for the SCH 697243 Drug Product.

11. Please provide complete OQ and PQ protocols and results for the following equipment:

(b)(4)

(b)(4)

(b)(4)

13. For the control of drug product, please provide the validation report for the Absence of Specified Microorganisms showing that test (section 3.2.P.5.2) was qualified in accordance with (b)(4) Please include the indicator microorganisms tested, to include their media and incubation conditions, and a copy of test (section 3.2.P.5.2).

14. For the control of drug product, please provide the validation report for the Microbial Enumeration showing that test (section 3.2.P.5.6) was qualified in accordance with (b)(4) . Please include the indicator microorganisms tested, to include their media and incubation conditions, and a copy of test (section 3.2.P.5.6).

15. We reconsidered one of the comments conveyed to you at the December 3, 2001, pre-IND meeting. At that time we stated that "labeling the product with units other than that currently used in the United States, would not be acceptable." We may now consider it acceptable to label a product in units other than those currently in use for US-licensed allergenic products, based on supportive data submitted in the BLA package. However, if a new product is licensed to be labeled in such units, we would expect lot release specifications to include a potency determination based on unit established for existing US standardized allergenic products, if possible. Furthermore, we expect that the package insert will include a description of this potency specification and its relationship to recommended dosing.

16. We have determined that the proper name of your product will be "Timothy Grass Pollen Allergen Extract" and the dosage form is "Tablet for sublingual use." Please revise the proper name and dosage form. Please note that labeling is not final until the BLA is approved. Please also note that the proper name and form and proprietary name are subject to change during labeling negotiations.

Please submit your response in a timely manner as an amendment to your BLA, so that we may continue the review of your application. If we determine that your response to this information request constitutes a major amendment, we will notify you in writing. If we receive your major amendment during the last three months of the review period, we will extend the review period an additional three months. We are continuing to review your application.

If you have any questions, please contact the Regulatory Project Manager, Dr. Juan Lacayo at (301) 796-2640.