(System Info - 240007 RIVERS KATIE 06/19/2013 08:07:49 RIVERSK)
Dear Scott,

We have the following information request for your BLA, STN125478/0:

In your BLA for Short Ragweed Pollen Allergen Extract, Tablet for Sublingual Use (Section 3.2.P.5.6, Section 7.0 (b) (4) ), you propose that the (b) (4) be monitored and controlled throughout the manufacturing process by (b) (4) . In addition, you state "Merck has concluded that no additional test is required at release to demonstrate (b) (4) . In a letter dated October 29, 2009, FDA agreed that this proposal was acceptable." The letter you reference was in response to a proposal under your IND 13143 in which you indicated that the (b) (4) be monitored by (b) (4) in accordance with ICH Q6A.

The agreement under the IND may have been in error for the following reasons:

a. As stated in FDA's Compliance Policy Guide (CPG) (b) (4) of Tablets and Capsules (b) (4) the FD&C Act requires that drug products which are not official (and therefore not subject to compendial requirements) nonetheless meet standards of strength and quality which they purport or are represented to possess. Current good manufacturing practice regulations (21 CFR 211.160) require the establishment of scientifically sound and adequate specifications to assure those product attributes. Specifications for (b) (4) are required, within this context, for non-official (non-compendial) tablets with less than 50 mg of any active ingredient. Tablets that are not tested for (b) (4) are therefore in violation of the FD&C Act. Specifications for the (b) (4) test may be in accordance with the (b) (4) (Chapter (b) (4)) or other scientifically sound alternative specifications may be used. Your tablets do not meet the requirements of the CPG or the current (b) (4) threshold for use of a (b) (4) t instead of a (b) (4) . Therefore, your proposal to demonstrate (b) (4) solely by monitoring of (b) (4) is not acceptable.

b. In support of your IND request for exemption from (b) (4) testing, you referenced ICH Q6A. Please note that ICH Q6A is for New Drug Substances and Drug Products; Chemical Substances. This guidance is applicable to new drug products of synthetic chemical origin and specifically excludes any high MW peptides and polypeptides and biologic or biotechnological products. In addition, you did not reference ICH Q4B Annex 6(R1) which provides regional opinions on (b) (4) testing. Therefore ICH Q6A cannot be used in support of your proposal for (b) (4) testing only for your tablets. In addition, it is unclear if ICH Q6A or some other guidance was used to support your proposal not to perform (b) (4) testing on final product. Your proposal to not perform any (b) (4) testing of the final drug product is not acceptable.

Due to the nature of your production process it appears that (b) (4) testing is appropriate at the final product stage. Please confirm the (b) (4) test will be added as a final product release test for your Short Ragweed Sublingual Tablets. Please provide the specifications you propose to use for this test and data from qualification studies in support of the test.

Please contact me if you have any questions.

Thank you,

Katie

Katie H. Rivers, M.S.
Regulatory Project Manager, CMC1
FDA/CBER/OVRR/DVRPA
1401 Rockville Pike, HFM-481
Rockville, MD 20852

Phone 301-796-2640
Fax 301-827-3532