RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125473/0 and 125478/0 Office: OVRR

Product: Timothy Grass Pollen Allergen Extract/Short Ragweed Pollen Allergen Extract

Applicant: Merck Sharp & Dohme Corp.

Telecon Date/Time: 08-Aug-2013 10:00 AM Initiated by FDA? Yes

Telephone Number:

Communication Categorie(s): 1. Advice

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Telecon Summary:
CBER sent an information request regarding (b)(4) testing to the sponsor on June 18, 2013. Merck responded in amendment 6 on July 19, 2013. The purpose of this telecon is to discuss Merck's reply and the need for (b)(4) testing on the final drug products.

FDA Participants:
Jay Slater
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Non-FDA Participants:
Merck
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Telecon Body:
CBER stated that they have reviewed Merck's response to the June 18, 2013, information request and consulted internally with CDER experts and high-level management. The proposed use of (b)(4) to test for (b)(4) is not sufficient; (b)(4) Testing is required according to (b)(4)

CBER explained that the justification for use of a (b)(4) test, as proposed with a (b)(4) , was not sufficient. There is not enough evidence to confirm that the product is a (b)(4) prior to freeze drying, and testing (b)(4) on the product in the final blister pack is not sufficient to show (b)(4) . Although the flow diagram explains the manufacturing process, there are multiple stages throughout manufacture where (b) (4) (b)(4) may occur. The drug product has been analyzed only using the (b)(4) test which, considering the nature of the product, is why the data may appear acceptable. However, the product will not be considered in compliance if (b)(4) testing is not performed.

CBER requested that the sponsor implement a (b)(4) test and stated that there are currently acceptable methods available to meet this requirement. CBER noted that the (b)(4) in (b)(4) may not work exactly for these types of products and that therefore it may be acceptable to (b)(4) to meet the needs of this product. CBER is also open to discussion regarding the (b)(4) . CBER asked if there is available European data for (b)(4) testing on GRASTEK. Merck stated that there is not a procedure in place for determining (b)(4) and therefore data are not available.

CBER requested that due to limited time frames, Merck get started working on implementing a procedure for (b)(4) testing as soon as possible. Merck thanked CBER for making their position and perspective clear, and questioned whether the (b)(4) test needs to be in place for testing of the launch batches. CBER expressed concern about this question; since the (b)(4) test can be performed using an assay that is already in place, Merck should be able to have a (b)(4) testing protocol approved before launch batches are due to be released. A new assay does not need to be developed and a large amount of launch lot product will not need to be sacrificed. CBER anticipates that implementing a procedure for (b)(4) testing will take weeks, while final lot release testing will not take place for months.

CBER asked if any (b)(4) testing has been previously performed and Merck responded that they have not completed any (b)(4) testing due to previous guidance that it was not required; however, they can implement the (b)(4) test. Merck questioned whether the (b)(4), proposed for (b)(4) testing, could be used for (b)(4) testing. CBER responded that this approach seems reasonable and asked that Merck send a proposal to CBER for review. CBER advised Merck to look at their data for appropriate measures of

components in the assay. CBER stated that Merck has two options, test for either (b)(4). Both the (b)(4) and the (b)(4) should be considered for (b)(4) testing; however, the (b)(4) requires (b)(4) and this may be an issue.

Merck stated that they plan to manufacture the launch lots beginning in (b)(4). CBER stated that multiple CMC information requests (IRs) are forthcoming, as appropriate at this point in the review cycle. Additional IRs may be sent by the facilities reviewer. CBER clarified that these requests may impact manufacturing actions. Merck stated that this timeframe is due to production of lots needed for CBER lot release. CBER encouraged the sponsor not to rush production because changes to manufacturing may be needed based on the IRs that CBER sends to Merck.

CBER noted that the need for (b)(4) testing will most likely also (b)(4), but a formal review has not yet been completed.

Merck stated that they understand the requirement for (b)(4) testing and will move forward and provide a proposal.

We thanked each other and the call ended.