



Our STN: BL 103738/5031

Mekos Laboratories AS
Attn: Bo Poulsen
Herredsvejen 2
3400 Hillerod
DENMARK

JUN 30 2006

Dear Mr. Poulsen:

This letter is in regard to your supplement to the T.R.U.E TEST BLA for a new panel containing five rubber related allergen patches (Carba Mix, Black Rubber Mix, Mercaptobenzothiazole, Mercapto Mix, and Thiuram Mix) plus a negative control to be manufactured at your Hillerod, Denmark location submitted under section 351 of the Public Health Service Act.

We have completed the review of all submissions made relating to this BLA supplement. In our review, we find that the information and data submitted are inadequate for final approval action based on the deficiencies outlined below.

1. In Attachment 17, you proposed a new specification for future assessment of (b) (4) content uniformity data. In the current approved specification, (b) (4) analyses are performed, with (b) (4) failures (outside the (b) (4) limit but within the (b) (4) limit) permitted. According to the proposed specification, (b) (4) analyses will be performed for each allergen product, with (b) (4) failures permitted. Based on a Poisson distribution, the 95% upper confidence limit for (b) (4) failures is (b) (4) failures, or (b) (4). However, the 95% upper confidence limit for (b) (4) failures is (b) (4) or (b) (4). Please revise the new specification to make the 95% upper confidence limit for failure in the proposed specification consistent with the existing one.
2. Expiration dating will be based upon real-time stability data of the final assembled product in the proposed configuration. Please provide stability data for the final assembled rubber panel product.
3. Please provide a lot release protocol for the new rubber panel. In addition, you will need to submit samples of the first production lot along with analytical standard raw materials to CBER for CBER lot release testing. Please acknowledge.

4. In attachment 20, “determination of black rubber mix in T.R.U.E.TEST”, appendix 1, the (b) (4) of black rubber mix sample has (b) (4). Likewise, in the same attachment in “determination of mercaptobenzothiazole in T.R.U.E. TEST”, appendix 1, the (b) (4) of mercaptobenzothiazole sample has (b) (4). Please explain.
5. In attachment 20, at the bottom of page 2(8), the unit of concentration of black rubber mix standard (b) (4) should be (b) (4) instead of μg . Likewise, on page 2(7), the unit of concentration of thiuram mix standard (b) (4) should be (b) (4) instead of μg . Please correct.
6. We reserve comment on the proposed labeling until the supplement is otherwise acceptable.

Within 10 days after the date of this letter, you should take one of the following actions: (1) amend the supplement; (2) notify us of your intent to file an amendment; (3) withdraw the supplement; or (4) request a hearing on the grounds for denying approval of the supplement.

We stopped the review clock with the issuance of this letter. We will reset and start the review clock when we receive your complete response.

If you have any questions, please contact the Regulatory Project Manager, Ms. Jennifer Ross, at (301) 827-3070.

Sincerely yours,

/s/

Richard I. Walker, Ph.D.
Director
Division of Bacterial, Parasitic
and Allergenic Products
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research

cc: James Kenimer, Ph.D.
The Biologics Consulting Group, LLC