

## Memorandum of Meeting Minutes

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Meeting Date: February 15, 2002

Time: 9:30 a.m.

Location: Corporate Building, Conference Room S300

Type of Meeting: Feedback Meeting

Subject: Inclusion of Phenylephrine Bitartrate as an Active Ingredient in the "Cold, Cough, Allergy, Bronchodilator, Antiasthmatic Drug Products For Over-the-Counter Human Use; Final Monograph for OTC Nasal Decongestant Drug Products" (Docket No. 76N-052N).

Meeting Recorder/Project Manager: Babette Merritt

### FDA Participants:

Jonca Bull, M.D., Acting Director, Office of Drug Evaluation V  
Charles Ganley, M.D., Director, Division of Over-the-Counter Drug Products (DOTCDP)  
Linda M. Katz, M.D., Deputy Director, DOTCDP  
Marina Chang, R.Ph., Team Leader, DOTCDP  
Michael Benson, P.D., J.D., Regulatory Review Pharmacist, DOTCDP  
Gerald Rachanow, P.D., J.D., Regulatory Counsel, DOTCDP  
Andrea Leonard-Segal, M.D., Medical Officer, DOTCDP  
Robert Sherman, Regulatory Review Biologist, DOTCDP  
Cathy Vaughn, Pharmacy Student, DOTCDP  
Elaine Abraham, R.Ph., Project Manager, DOTCDP  
Robert J. Meyer, M.D., Director, Division of Pulmonary and Allergy Drug Products (DPADP)  
Charles E. Lee, M.D., Medical Officer, DPADP  
Emmanuel Fadiran, Team Leader, DPADP  
Bill McConagha, J.D., Regulatory Counsel, Office of General Counsel (OGC)  
Babette A. Merritt, Project Manager, DOTCDP

### Bayer Corporation Participants:

Harry Cocolas, Ph.D., Senior Associate Director, Formulations Development  
Randy Koslo, Ph.D., Director, Medical Affairs and Clinical Research  
Joanne Robinett, Director, Regulatory Affairs  
Mary Rose Salvacion, Manager, Regulatory Affairs  
Andrew Snoddy, Ph.D., Senior Associate Director, Clinical Research  
R. William Vander Haar, Ph.D., Senior Vice President Global Scientific Affairs

Background: Bayer Corporation requested this meeting to discuss the inclusion of phenylephrine bitartrate in the Cold, Cough, Allergy, Bronchodilator and Antiasthmatic Drug Products for Over-the-Counter Human Use Monograph as a nasal decongestant. Bayer has proposed that demonstration of bioequivalence of a single ingredient phenylephrine bitartrate formulation to a single ingredient phenylephrine hydrochloride preparation (at the dose under the current monograph) should be sufficient to establish the inclusion of phenylephrine bitartrate in the final monograph.

Discussion:

Bayer presented the following questions :

- *Does the Agency agree the demonstration of in-vitro and in-vivo comparability has been established? Is the Agency in agreement to including phenylephrine bitartrate as a GRASE ingredient in the Oral Nasal Decongestant Final Monograph for effervescent formulations?*

The Agency agrees that it appears that *in-vitro* and *in-vivo* comparability have been demonstrated. However, bioequivalence between the formulations needs to be demonstrated according to the Agency's Guidance for Industry: Bioavailability and Bioequivalence Studies for Orally Administered Drug Products General Considerations. The applicant needs to supply the Agency with a full report including complete bioequivalence analysis.

- *Are the market place data adequate to support the material time and extent criteria needed to categorize phenylephrine bitartrate a GRASE ingredient and for inclusion into the Nasal Decongestant Final Monograph for formulation with effervescent formulations?*

The Agency would like Bayer to present the marketplace data from OTC marketing outside the U.S. The marketplace data should be provided in the applicant's submission to the Agency. This data, in conjunction with the demonstration of bioequivalence, may be adequate to establish phenylephrine bitartrate as GRASE.

Additional Discussion:

- The Agency suggested that a more expeditious way to get the reformulated product to market may be to file a 505(b)(2) NDA. However, this application would need to include a stability profile, normally required under an NDA. Bayer noted that it had 6 products that would be reformulated to contain phenylephrine bitartrate, and asked if the data were sufficient for monograph status. The Agency replied that it had not fully resolved the material time and extent issues or what would constitute an adequate safety profile because the ingredient had not been marketed in the U.S. for over 25 years. The Agency stated that inclusion in the monograph would involve notice and comment rulemaking, and that interim marketing would be unlikely.

- The Agency asked the applicant how much foreign marketing history is available for this ingredient. Bayer stated that it has years of foreign marketing experience and products are still on the market in other countries.
- The Agency clarified that the panel report published in 1976 listed phenylephrine bitartrate among the labeled ingredients in marketed products but did not include any evaluation of phenylephrine bitartrate. The Agency does not know why the panel did not look at this any further.

Conclusion:

- Bayer will submit a full report to demonstrate the bioequivalence of phenylephrine bitartrate to a reference phenylephrine hydrochloride formulation for the Agency's evaluation.
- Bayer will submit an integrated safety summary based on its foreign marketing data and include it with the final pK study.
- Bayer needs to decide whether it wants to proceed under a 505(b)(2) NDA or a petition to amend the monograph. All data should be submitted at one time for the Agency to review.

Action Item:

- Bayer will decide whether it is submitting a 505(b)(2) NDA or a petition (which would include the data listed under the conclusion above). Depending on the outcome of that decision it will submit the appropriate data.

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Babette Merritt, Project Manager  
Minutes Preparer

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Gerald Rachanow, P.D., J.D.  
Regulatory Counsel  
Concurrence

Cc: List of Attendees  
HFD-560 Division Files  
HFA-305, Dockets Management (Docket No. 76N-052N)

Filename: phenyl.eph.fdbkmtg.2.15.02

Prepared: B. Merritt, 2/15/02