Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Memorandum of Facsimile Correspondence

Date: May 19, 2008

To: Richard Fosko, R.Ph., MPH
Director, Regulatory Affairs

Company: Meda Pharmaceuticals

Fax: 732-564-2361

Phone: 732-564-2358

From: Philantha Bowen, MPH, RN
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: IND 77363; Re: SPA Meeting Minutes

# of Pages including cover: 10

Thank you.

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Meeting Type:	Type A
Meeting Category:	Special Protocol Assessment
Meeting Date and Time:	April 29, 2008 9:00-10:00 AM
Meeting Location:	Building 22, Conference Room 1415
Application Number:	IND 77,363
Product Name:	Azelastine Hydrochloride and Fluticasone Propionate Nasal Spray
Received Briefing Package	April 15, 2008
Sponsor Name:	MEDA Pharmaceuticals
Meeting Requestor:	Richard Fosko, R.Ph., MPH Director, Regulatory Affairs
Meeting Chair:	Badrul A.Chowdhury, M.D., Ph.D., Director Division of Pulmonary and Allergy Products
Meeting Recorder:	Philantha M. Bowen, MPH, R.N. Sr. Regulatory Management Officer

Meeting Attendees:

FDA Attendees

Office of Drug Evaluation II

Badrul A. Chowdhury, M.D., Ph.D., Division Director, Division of Pulmonary and Allergy Products

Philantha Bowen, M.P.H., RN, Sr. Regulatory Management Officer, Division of Pulmonary and Allergy Products

Sally Seymour, M.D., Clinical Team Leader, Division of Pulmonary and Allergy Products

C. Joe Sun, Ph.D., Pharmacology/Toxicology Team Leader, Division of Pulmonary and Allergy Products

Jean Wu, M.D., Ph.D., Pharmacology/Toxicology Reviewer, Division of Pulmonary and Allergy Products

Office of New Drug Quality Assessment

Prasad Peri, Ph.D., Pharmaceutical Assessment Lead, Division of Pre-Marketing Assessment I, Branch II

Eugenia Nashed, Ph.D., Quality Reviewer, Division of Pre-Marketing Assessment I, Branch II

Office of Clinical Pharmacology

Wei Qiu, Ph.D., Acting Clinical Pharmacology Team Leader, Division of Clinical Pharmacology 2

Sponsor Attendees

Richard Spivey, PharmD, Ph.D., Senior Vice President, Research and Development

Harry Sacks, M.D., Vice President, Medical and Scientific Affairs

Cary Sax, Associate Director, Regulatory Affairs

Warner Carr, MD, Consultant

Phillip Lieberman, MD, Consultant

1.0 BACKGROUND

MEDA Pharmaceuticals submitted a Special Protocol Assessment (SPA) dated December 21, 2007, for the clinical protocol MP4002 for the azelastine/fluticasone combination nasal spray. On January 31, 2008, the Division responded to MEDA's SPA request.

MEDA Pharmaceuticals submitted a Type A meeting request, dated February 29, 2008, to discuss the Agency's comments and responses regarding the SPA. The briefing package, dated April 14, 2008, was reviewed by the Division. On April 28, 2008, the Division responded to MEDA's questions via facsimile. The content of the fax is printed below.

Any discussion that took place at the meeting is captured in section 3.0 including any changes in our original position. MEDA's questions are in ***bold italics*** and FDA's response is in *italics*; the discussion is in normal font.

2.0 QUESTIONS

2.1 QUESTION 1

Question 1:

Does the Division agree that patients with moderate/severe nasal symptoms of seasonal allergic rhinitis, as defined by ARIA, is an appropriate target population for this drug?

Division Response:

We do not agree. We have expressed concerns that you have not provided evidence that a population for this combination product exists. The ARIA Guidelines presented do not alleviate these concerns. The ARIA classification for allergic rhinitis classifies allergic rhinitis based upon intermittent and persistent symptoms and is not universally adopted in the United States. In particular, this type of classification is not used for approval of therapeutics for allergic rhinitis.

The combining of different products to control symptoms of SAR is the practice of medicine. Single ingredient products containing azelastine or fluticasone propionate are approved for treatment of symptoms of seasonal allergic rhinitis. The combination product that you are proposing to develop is targeted to treat the same symptoms that the single ingredient products are already indicated for. Demonstrating significantly greater symptom relief with the combination product over its individual single active ingredients will not be sufficient to demonstrate that both azelastine and fluticasone propionate contribute to the effectiveness of the combination. Demonstration of greater symptom relief with the combination product over its active ingredients (for the exact same symptoms) is likely to be due to the fact some patients may not be responding to

azelastine while responding to fluticasone propionate, and vice versa. Rationale based on pharmacodynamic reasoning, such as mechanism of action, onset of symptom relief, etc., are also not sufficient to justify this combination product.

As stated before, combining products eliminates flexibility with dosage titration and potentially exposes patients to unnecessary medication; and thus unnecessary risk.

2.2 QUESTION 2

Question 2:

Does the Division agree that our proposed inclusion/exclusion criteria will study a population of patients with moderate/severe rhinitis?

Division Response:

We do not agree. We do not have specific criteria using the TNSS to define what constitutes moderate or severe allergic rhinitis.

2.3 QUESTION 3

Question 3:

Does the Division agree that the proposed dosage of the individual components of the fixed dosage product (that are within the labeling for those marketed products) is appropriate for study in the MP4002 study?

Division Response:

We remain concerned about the lack of flexibility of dosage titration with the fixed dose combination (FDC). We acknowledge your explanation and ask you to make the reasoning in the NDA, if you are to develop this product. This will be a review issue.

2.4 QUESTION 4

Question 4:

Does the Division agree that no new corticosteroid-specific safety issues are anticipated with the fixed dose combination product that would require MEDA to study a dosage that is lower than the recommended dosage in the fluticasone label? This question is predicated on the assumption that adequate pK studies do not show

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