Final Minutes

October 19, 2000
Nonprescription Drugs Advisory Committee

Food and Drug Administration
Center for Drug Evaluation and Research
Holiday Inn, 2 Montgomery Avenue, Gaithersburg, MD

Safety Issues of Phenylpropanolamine (PPA) in Over-the-Counter Drug (OTC) Products

The meeting was held at the Holiday Inn, Gaithersburg, MD. Prior to the meeting, the members, consultants and guests reviewed background material from the FDA, from the Hemorrhagic Stroke Project conducted by Yale investigators and also material which the Consumer Healthcare Products Association had submitted for the committee's review. In order for the public to be informed, the background material was also available on the Dockets page the day before the meeting. There were approximately 150 persons in attendance. The meeting started at 8 a.m. and ended at 4:00 p.m.

Attendance:
NDAC Members Present: Eric Brass, M.D., Ph.D., Chair, Richard Neill, M.D., Edwin Gilliam, Ph.D., Julie Johnson, Pharm.D., Hari Sachs, M.D., Louis Cantilena, M.D., Ph.D., Francis Lam, Pharm.D., Donald Uden, Pharm.D., Henry Williams, M.D., George Blewitt, M.D.(non-voting)

NDAC Members Absent: Edward Krenzelok,

Consultants: Statisticians and Epidemiologists: Ralph D'Agostino, Ph.D., Janet Daling, Ph.D.; Janet Elashoff, M.D., **Neurologists:** Sid Gilman, M.D., **Consumer Rep:** Susan Cohen

Non-voting Guest: Epidemiologist: Steven Kittner, M.D., MPH; **Neurologist:** Steven Warach, M.D., Ph.D.

FDA Participants: Janet Woodcock, M.D., Robert DeLap, M.D., Ph.D., Charles Ganley, M.D., Linda Katz, M.D., MPH, Robert Sherman, Lois La Grenade, M.D., MPH.

Open Public Hearing: Three presentations
Brian Strom, M.D., MPH, University of Pennsylvania representing Whitehall Corporation;
David E. Schteingart, M.D., University of Michigan representing Chattem;
Sidney Wolfe, M.D., Director, Public Citizen's Health Research Group

Historical Overview
Robert L. Sherman, DOTCDP, described the Regulatory History of OTC PPA.

Yale Presentation
Walter Kernan, M.D. presented the Final Report of the Hemorrhagic Stroke Project (HSP). The committee asked clarification questions following the presentation.

Consumer Healthcare Products Association
The Consumer Healthcare Products Association had several speakers who made comments about the HSP. R. William Soller, Ph.D., Senior Vice President and Director of Science and Technology CHPA; Noel S. Weiss, M.D., Dr. P.H., University of Washington; Lewis Kuller, M.D., Dr. Ph.H.; Robert B. Wallace, M.D., Philip B. Gorelich, M.D., Charles H. Hennekens, M.D., Dr. P.H., University of Miami School of Medicine. NDAC asked clarification questions following all of these statements.

FDA
Lois La Grenade, M.D., M.P.H., OPDRA, presented her Divisions epidemiological analysis of the agencies post marketing data on risks related to PPA, and presented a critique of the HSP. Charles Ganley, M.D., Director, DOTCDP gave an overview on how the FDA views safety issues and how the deliberations today would contribute to bringing closure to the PPA rulemaking.

Committee Discussion and Vote:
Following these presentations the committee discussed issues before beginning the vote on the following questions. The Chair revised question A and the subparts:

Questions Related to the Results and Interpretation of the Hemorrhagic Stroke Project :

A. Do the results from the HSP study for subjects in the 18 – 49 years of age

suggest that PPA is **safe** from risk of hemorrhagic stroke,
suggest that there is an **association** between PPA and hemorrhagic stroke,
or are **inconclusive.**

1. For females 18 – 49 using PPA as appetite suppression

   0=Safe 13=Association 1=Inconclusive

2. For females 18 –49 using PPA as decongestants

   0=Safe 6=Association 8=Inconclusive

3. For females 18 –49 using PPA on first exposure

   0=Safe 13=Association 1=Inconclusive

4. For Men 18-49 using PPA as appetite suppression

0=Safe 0=Association 14=Inconclusive

5. For Men 18-49 using PPA as decongestant

0=Safe 0=Association 14=Inconclusive

6. For Men 18-49 using PPA on first exposure

0=Safe 0=Association 14=Inconclusive

7. For the entire population (men and women) using PPA as appetite suppression

0=Safe 13=Association 1=Inconclusive

8. For the entire population (men and women) using PPA as decongestant

0=Safe 5=Association 9=Inconclusive

9. For the entirel population (men and women) using PPA on first exposure

0=Safe 13=Association 1=Inconclusive

B. Does the HSP provide information on which populations may be at greater or lesser risk?

The issue was discussed, and members pointed out the limitation of subgroup data.

Questions Related to the Availability of PPA in the OTC Market.

C. There is a body of data collected over the years that has suggested a possible association between PPA use and hemorrhagic stroke. Taking all currently available information into account, do the data support the conclusion that:

1. There is not an association between PPA use and hemorrhagic stroke?
2. There is an association between PPA use and hemorrhagic stroke?
3. The association still remains uncertain because of insufficient information?

0=no association 13= Yes Association 1=uncertain

D. Considering your answer to question C, can PPA be considered to be generally recognized as safe for use as:

1. a decongestant ?

0=Yes 12 = No 2=Abstain

2. an appetite suppressant?

0=Yes 13=No 1=Abstain

a) When answering this question, please address whether dose is an important consideration.

During the discussion, members could not conclude there was any dose relationship however they did think there was some evidence to suggest this relationship.

In making the risk/benefit analysis the following comments were made:

What does the consumer loose if is taken off the market?

One member stated that when a drug is only marginally useful, any degree of risk is much less tolerable.

In discussing appetite suppression: In the long term 95% of people gain the weight back. Since there is no study on long-term use and the short term benefits for weight reduction are marginal no risks are acceptable. Regarding PPA for coughs many members felt here are other products that are equally good and that do not have this risk profile.

It was pointed out that the PPA study was in reality similar to an actual use study because it described how consumers use products. It was troubling that a high proportion of subjects were hypertensive and were taking PPA. This indicates that labeling alone could not be relied upon to communicate warnings.

Another member pointed out that the dose that seems to be causing the problem is not a massive overdose and so it becomes doubtful if one could effectively label or expect that consumers would follow the label.

A verbatim transcript of this meeting will be available on the FDA's Dockets Management Branch Website approximately 30 days after the meeting. The address is HTTP://www.fda.gov/ohrms/dockets/ac/acmenu.htm.

I certify that I attended the October 19, 2000 meeting of the Nonprescription Drugs Advisory Committee and that these minutes accurately reflect what transpired.

Sandra Titus 11/1/00
Sandra Titus, Ph.D. Date
Executive Secretary, NDAC

11/13/00
Eric Brass, M.D., Ph.D. Date
Chair, NDAC