

**Meeting of the Nonprescription Drugs Advisory Committee  
September 25, 2006**

This is the final report of the Nonprescription Drugs Advisory Committee Meeting held on September 25, 2006. A verbatim transcript will be available in about 2 weeks, sent to the Division and posted on the FDA website at <http://www.fda.gov/ohrms/dockets/ac/cder05.html#NonprescriptionDrugs>

All external requests for the meeting transcripts should be submitted to the CDER Freedom of Information office.

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The Nonprescription Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on September 25, 2006 at the Hilton Washington D.C. North/Gaithersburg the Ballrooms, 620 Perry Parkway, Gaithersburg, Maryland. Eric Brass, M.D., PhD chaired the meeting. There were approximately 175 in attendance.

**Attendance:**

**Nonprescription Drugs Advisory Committee Member:**

Ernest B. Clyburn, MD; Jack E. Fincham, PhD; Ruth M. Parker, MD; Robert E. Taylor, MD, PhD, F.A.C.P;

**Nonprescription Drugs Advisory Committee absent Members**

Terrence G. Blaschke, MD; Mary E. Tinetti, MD

**Consultants (voting):**

Neal Benowitz, MD; Eric P. Brass (Acting Chair); Louis Cantilena, MD; Ralph B. D'Agostino, PhD; Ruth S. Day, PhD; Terry C. Davis, PhD; Marie R. Griffin, MD; Richard A. Neill, MD; Wayne R. Snodgrass, MD, PhD; Musa J. Mayer, M.S. (Patient Representative)

**Guest Speakers (non-voting)**

Saul Shiffman, PhD; Alastair Wood, MD

**Industry Representative: (non-voting):**

George S. Goldstein, MD

**FDA Participants:**

Charles Ganley, MD, Andrea Lenoard-Segal, MD

**Open Public Hearing Speakers:**

Sujit S. Sansgiry, PhD, University of Houston

Julie Aker, President & CEO, Concentrics Research

Douglas Ws. Bierer, Douglas Bierer Consulting, LLC

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On September 25, 2006, the committee discussed issues related to the analysis and interpretation of consumer behavior studies conducted to support marketing of nonprescription drug products.

Eric Brass, MD, PhD, (Acting Chair), called the meeting to order at 8:00 a.m. The Committee members, consultants, and FDA participants introduced themselves. The conflict of interest statement was read into the record by Darrell Lyons, BSN, Designated Federal Officer (DFO) the agenda preceded as follows:

- 8:00 Call to Order  
Introduction of Committee Members
- Conflict of Interest Statement
- 8:30 Welcome and Opening Comments
- FDA Presentations:**
- 8:50 Health Literacy
- 9:20 Consumer Behavior Studies
- 9:50 Break
- 10:05 Information Processing
- 10:35 Statistical Considerations
- 11:05 Complexities of the Rx to OTC Switch
- Eric Brass, MD, PhD**  
Acting Chair, Nonprescription Drugs Advisory  
Committee, NDAC
- LT Darrell Lyons, BSN**  
Designated Federal Official, NDAC
- Andrea Leonard-Segal, MD, Director**  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products, FDA
- Ruth Parker, MD**  
Professor of Medicine  
Department of Medicine, Emory University  
School of Medicine  
Atlanta, GA
- Terry Davis, PhD**  
Professor,  
Health Science Center-Shreveport  
Louisiana State University  
Shreveport, LA
- Saul Shiffman, PhD**  
Professor,  
Department of Psychology  
University of Pittsburgh  
Pittsburgh, PA
- Ruth Day, PhD**  
Director,  
Medical Cognition Laboratory and Director,  
J.D. /M.A. Program, Duke University
- Ralph D'Agostino, PhD**  
Professor,  
Boston University  
Boston, MA
- Alastair Wood, MD**  
Vanderbilt Medical School  
Nashville, TN

11:35 Final Questions from the Committee to the Speakers

12:00 Lunch

1:00 Open Public Hearing

2:00 Break

2:15 Committee Questions/Discussion

5:00 Adjourn

### Questions to the Committee:

#### Design, Statistical Considerations and Study Conduct

- I. There are no clear guidelines regarding the number of people that should be enrolled into label comprehension, self-selection, and actual use studies. Please discuss the sample size that should be used in each type of study and describe the basis for your response.
  - a. In some applications, there is a need to be assured that certain populations at risk for serious harm are excluded from using the drug. We often ask for a self selection study in a group of these patients to assess whether they may consider using the drug. Please describe what sample size should be considered for these types of studies.

#### **Committee Discussion:**

The committee recommended for the three types of studies, (label comprehension, self selection and actual use) that sponsors clearly state the objectives and domains of interest i.e. specific consumer behavior(s) of primary interest, contact with physician, appropriate use etc. Each objective should have a prospectively specified quantitative definition of success, based on point estimates, 95% confidence intervals or other criteria. Objectives and quantitative targets may be discussed with the FDA prior to study initiation. Based on these quantitative objectives appropriate sample size can be determined with standard techniques.

*(See Transcript for Complete Discussion)*

2. Please discuss how the data from consumer studies should be presented for interpretation with regard to point estimates, confidence intervals, or statistical measures.
  - a. Can a threshold of success be defined where anything above the threshold is considered some guarantee that the sponsor met the standard for switch? Please discuss when this should be considered, for what types of studies and how we should determine at what level of success (e.g. 75%, 95%).

#### **Committee Discussion:**

The committee agreed that thresholds could, and in most cases should, be defined however; several Committee members felt that the thresholds would vary depending upon the individual and public health implications of each specific question.

*(See Transcript for Complete Discussion)*

3. In assessing the ability of consumers to self select, it is often difficult to ask the question without the potential for biasing the answer. Please discuss how self selection may be ascertained with minimal bias to the consumer.

And
4. Many companies want to use purchase decisions as the metric for assessing self selection. FDA has refrained from using this metric because there may be other factors that influence the decision which may be totally unrelated to the consumer understanding the label (e.g. lack of interest in the product, cost). How should this type of data be viewed by FDA in the assessment of self selection?

**Committee Discussion: (question 3 & 4 was discussed together)**

The use of purchase vs. self-selection decisions as endpoints each has negative and positive aspect. The Committee felt that the self-selection was the most conservative estimate of consumer behaviors. The Committee discussed “Discrete Choice” analysis as an additional tool to understand the basis of decisions which may be influenced by many factors. (See Transcript for Complete Discussion on both questions)

5. It can be difficult to verify specific aspects of a self-selection decision. For example, verification of a consultation with a participant’s personal doctor can be burdensome. Under what circumstances is it necessary to verify these components of the self-selection decision and how should verification be accomplished?

**Committee Discussion:**

The Committee noted that the more objectively that a study is conducted in terms of verifying responses the better the quality of the study. Verification of key behaviors such as contacting of a physician should be used when such behaviors are critical to the safe and effective use of a potential OTC drug. (See Transcript for Complete Discussion)

6. Consumer behavior studies are generally open label single arm studies. Discuss under what circumstances FDA should request that multiple arm studies be considered whereby the differences in the arms reflect a comparison of different labels or differences in ancillary measures (e.g. package insert versus no package insert). (See Transcript for Complete Discussion)
7. OTC products may be used intermittently, or have limits on the duration of continuous use (e.g. internal analgesics have 10 day limit for pain treatment), or have a set period of use to achieve clinical benefit (e.g. nicotine replacement products). Please discuss the factors that should be considered in determining the duration of actual use studies. (See Transcript for Complete Discussion)

Labeling

1. How should we determine which information is essential for self-selection and use and therefore must be on the Drugs Facts Label and what information could be provided in a package insert?

**Committee Discussion:**

The Committee agreed that The Drug Fact Label must contain all of the information that is essential in making the initial self-selection; other informative package inserts should be deemed supplementary information. There was also some discussion, in general, as to placing some limits to the information provided on the Drug Fact Label. (See Transcript for Complete Discussion)

Data Analysis and Interpretation

1. Some products may have multiple criteria for a consumer to consider when determining whether they are eligible to use the product (e.g. cholesterol lowering agents). What standard should be applied when interpreting self-selection data for these types of products?

**Committee Discussion:**

The discussion highlighted two approaches. Some Committee members felt that quantitatively strict criteria should be used for the assessment of all label elements. Other members felt that the criteria should vary based on the importance of the message and the implications of non-heeding. Additionally, some members felt that from a public health standpoint it is important to not only consider whether or not it is safe to self-select but, whether it is appropriate to self-select. Economically, self-selection could affect those with limited means. (See Transcript for Complete Discussion)

2. Companies often want to include responses as being correct, even though they do not conform exactly to the labeled information. How should these types of responses be evaluated in the assessment of consumer behavior? If they are going to be permitted, should they be pre-specified in the protocol of the study?

**Committee Discussion:**

The Committee agreed that analyses that allow incorrect behavior that is deemed correct (e.g. “acceptable”) must be pre-specified and built into the analysis. A complete error analysis of all data on all questions to see the range of type of errors that were committed would typically also be helpful.

*(See Transcript for Complete Discussion)*

3. How should data from low literate subjects be evaluated relative to data from the general population of subjects included in the studies? Alternatively, should FDA just require a certain percentage of low literate subjects be included in the study and conduct analysis only on the whole population?

*(See Transcript for Complete Discussion)*

4. What type of information can provide more confidence that these studies are predictive of

The committee agreed that more research is needed about consumer behavior in the marketplace, as well as phase 4 studies that look at key issues to ensure that the behavior predicted in clinical trials occur in the marketplace and to identify any substantial safety concerns for the public health.

*(See Transcript for Complete Discussion)*

The meeting was adjourned at approximately 4:40 p.m. on September 25, 2006.

October 18, 2006  
Nonprescription Drugs Advisory Committee

These summary minutes for the September 25, 2006 Meeting of the Nonprescription Drugs Advisory Committee of the Food and Drug Administration were approved on October 18, 2006.

I certify that I attended the September 25, 2006, Meeting of the Nonprescription Drugs Advisory Committee of the Food and Drug Administration meeting and that these minutes accurately reflect what transpired.

\_\_\_\_\_/s/\_\_\_\_\_  
Darrell Lyons, BSN  
Designated Federal Officer

\_\_\_\_\_/s/\_\_\_\_\_  
Eric Brass, MD, PhD  
Acting Chair, NDAC