Memorandum

Department Of Health and Human Services
Food and Drugs Administration
Center For Drug Evaluation and Research
Division of Over-the-Counter Drug Products (HFD-560)

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Subject: Consumer Behavior Issues Related To the Marketing of Mevacor OTC

To: Joint Nonprescription Drug / Endocrinologic and Metabolic Drugs Advisory Committee scheduled to meet on January 13 and 14, 2005

The proposal to market Mevacor OTC raises many issues that are different from the typical drug considered for OTC marketing. Most OTC drug products are currently marketed to treat symptomatic conditions for short periods of time. The duration of therapy can vary from a single dose to use for up to several months. For many of these conditions, consumers can accurately identify the symptom and receive positive feedback if the symptoms resolve after ingesting medication (e.g. an internal analgesic relieves a headache or minor muscle pain).

The proposal to make Mevacor OTC does not follow this paradigm. Elevated cholesterol is not associated with symptoms. Before using Mevacor OTC, consumers will be required to make several judgments regarding age, the level of LDL-cholesterol (LDL-C), risk factors for cardiovascular disease and relative contraindications to appropriately select to use the product (self-selection). Regardless of whether they do this correctly or not, they will also have to make decisions regarding continuation of therapy (de-selection). There is no positive feedback related to symptomatic improvement. Positive feedback will have to come from a lower LDL-C level, which will require motivation on the part of the consumer to educate themselves and continue to get cholesterol testing. Unlike other OTC drug products, Mevacor OTC should be a chronic therapy with the duration of use determined by the response to therapy and the development of relative contraindications during use. This clearly puts a burden on users unparalleled by any currently marketed OTC product. Any person choosing to use Mevacor OTC will have to be highly motivated in order to use it according to labeled instructions.

When making a decision to allow OTC marketing of a drug product, consumer behavior regarding self-selection and use of the product, without the benefit of a health provider, becomes pivotal in the benefit/ risk assessment. To help understand the possible implications of Mevacor 20 mg OTC, the sponsor has conducted an actual use study (The Custom Study) and a label comprehension study. These studies attempt to provide information on how consumers may use Mevacor in the OTC setting. FDA review staff analyzed the results of these studies and their reviews are included in this

background package. FDA will present its analysis of these studies at the advisory committee.

Label Comprehension Study

Section 502 (c) of the Federal Food, Drug, and Cosmetic Act (the Act) requires that nonprescription drug labeling be "in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use" (21 U.S.C. 352 (c)). Regulations further require that labeling "state the intended uses and results of the product; adequate directions for proper use: and warnings against unsafe use, side effects, and adverse reactions in such terms as to render them likely to be read and understood by the ordinary individual, including individuals of low comprehension, under customary conditions of purchase and use." (21 CFR 330.10 (a)(4)(v)).

A label comprehension study assists in the development of labels for OTC drug products. They focus on specific communication directives and use several different techniques to evaluate the content and format of labels. Participants may be asked direct questions regarding specific language in a label or they may be presented with scenarios describing a situation and are asked whether the medication is appropriate for the individual described in the scenario. The label comprehension studies are often conducted to assist in the development of a label to be used in an actual use study. Based on prior FDA experience, successful label comprehension results are not always reflective of subsequent consumer behavior. Consumers may understand the content of a label but may exhibit behavior that is contrary to the labeled instructions because unforeseen factors contribute to the decision to use the drug. Failure of label comprehension studies to meet objectives, however, raise concerns about the ability of the label to adequately communicate.

Actual Use Study

New drugs and drugs previously available only via prescription continue to be introduced into the OTC market, where consumers make decisions as to whether or not the drug is appropriate for them to use (i.e. self-selection, de-selection). Actual use trials can provide information about the ability of consumers to self-diagnose their medical condition (appropriate self-selection) and use the product safely and effectively in accordance with the information on the label and/or other information tools without the assistance of a learned intermediary. This also includes the ability to stop the medication (appropriate de-selection) should drug related adverse events occur or if the drug fails to provide benefit. Because other factors other than label comprehension influence consumer behavior, the actual use study can be a better predictor of use if the drug becomes available OTC.

An actual use study attempts to mimic the OTC retail setting but there are limitations to the study designs because investigator interaction is necessary to conduct the study. They are not perfect in their predictive nature but they can be helpful in identifying potential problems that could lead to poor outcomes for some individuals. In the course of the deliberations of the Mevacor OTC application, the advisory committee members will need to determine whether the success and failure rate for specific objectives in the actual use study support the marketing of Mevacor OTC.

The Custom Study

The Custom study is fairly straight forward in its design but is complicated by the presentation of various analyses. It is important to understand the details of the study protocol (described in the FDA and sponsor background material) and differentiate between the various analyses, what each mean and what the implications of each may be in the real world. In the presentation of material in the background packages and at the meeting, the definitions of various analysis groups or endpoints should be clear and unambiguous.

It is important to recognize that it is difficult to achieve 100% success when it comes to the correct use of a drug product in the OTC setting. In the course of the discussions of the study, it will be important for the members to consider the following:

- How efficacious is the drug likely to be for the individual patient?
- What are the risks of using the drug for the individual patient (when used according to labeled directions or when label is misinterpreted)?
- Are there certain subgroups that warrant greater concern because of increased risk for adverse events?
- What is the risk/benefit for an individual patient or a specific subpopulation of consumers who might use the product?
- What is an acceptable threshold for success and failure for the various objectives in the study?
- For a population who fails to correctly exclude themselves from using the product, can a projected benefit override the failure of self selection?