Discussion Points

1. Taking into consideration the efficacy data from the AFCAPS/TexCAPS and EXCEL studies, plus any additional information provided by the sponsor, please respond to the following questions:

    a. Does the proposed target population merit treatment with a statin to lower cholesterol and thereby reduce heart disease risk?

    b. Has the sponsor provided adequate rationale for the use of a fixed dose of lovastatin 20 mg to lower cholesterol and heart disease risk in this population (e.g. will a sufficient proportion of the population be able to reach an LDL less than 130 mg/dl)?

2. Are the safety and tolerability characteristics of lovastatin 20mg acceptable for an OTC drug? Consider the following questions:

    a. Lovastatin and other statins cause elevations in hepatic transaminase serum levels of unknown clinical significance in individuals with normal baseline hepatic function.

        i. Has the sponsor provided adequate justification for not requiring LFT monitoring in the OTC setting?

        ii. Has the sponsor addressed the extent to which a population with undiagnosed liver disease may be exposed to lovastatin 20 mg in the OTC setting?

        iii. Has the potential hepatic risk of lovastatin 20 mg in individuals with liver disease been adequately addressed?

    b. Statins cause muscle toxicity. Furthermore, drug-drug interactions with lovastatin may increase the risk of muscle toxicity. Is the risk of muscle toxicity with lovastatin 20 mg acceptable for an OTC drug?

    c. Lovastatin and other statins are currently labeled as Pregnancy Category X (the drug should not be used during pregnancy). Has the spectrum and magnitude of fetal toxicity with lovastatin 20 mg been adequately studied? Is the risk acceptable for an OTC drug?

Taking into consideration the results from the CUSTOM actual use study and the safety and tolerability characteristics of lovastatin 20 mg:

3. Does the frequency of appropriate self-diagnosis and self selection (screening into treatment based on labeled eligibility criteria) support the conclusion that lovastatin 20 mg can be used safely and effectively in the OTC setting?

4. A high percentage of study subjects in the CUSTOM actual use study relied upon a physician for correct self-selection and/or self-diagnosis. Given this, do the CUSTOM actual use study results support a conclusion that individuals without physicians can use lovastatin 20 mg safely and effectively in the OTC setting?

5. Do the results regarding self management (i.e. user behavior after the initiation of treatment) raise concerns about the safe and effective use lovastatin 20 mg in the OTC setting? If yes, what are these concerns?

6. The sponsor has a proposed a "self-management system" as part of the labeling (e.g. post purchase consumer assistance program) which would assist consumers in the use of the product. Has information been provided that these measures provide added value in consumer use of Mevacor?

Based on all the information provided:

7. Should a fixed dose of lovastatin 20 mg be marketed OTC for the proposed target population?

    a. If no, please describe the deficiencies and what the sponsor should do to gain OTC marketing approval?
    b. If yes, should the sponsor's "Self-management System" be a condition for approval? What other measures would you recommend?