CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-387

Pharmacology Review(s)

NDA 21-387

PHARMACOLOGY/TOXICOLOGY LABELING REVIEW

C.A. Resnick, Ph.D.

SPONSOR: Bristol-Myers Squibb
Princeton, NJ

FDA Liaison: Porter Layne, Ph.D.

PRODUCT: Pravastatin Sodium (40 mg) Tablets Co-packaged with Buffered Aspirin (81 or 325 mg mg) Tablets

INDICATION: Clinically Evident Coronary Heart Disease (to reduce the risk of death, nonfatal MI, myocardial revascularization procedures and ischemic stroke in these patients).

ORIGINAL SUBMISSION DATE: 22 June 2001
CENTER RECEIPT DATE: 22 June 2001

INTRODUCTION: This is an application to market two currently approved drugs (Pravachol and Bufferin), co-packaged for convenience[1]. The NDA does not contain a non-clinical pharm/tox section The sections of the package insert that refer to non-clinical studies appear to have been taken directly from the package insert for Pravachol and the professional labeling for aspirin.

EVALUATION: Other than a labeling review, a pharmacology/toxicology review is not needed for this application. As marketed drugs will be copackaged for administration to patients for whom those drugs are currently approved, there are no safety issues to be addressed and the application is approvable As for labeling, we have the following comments and recommendations regarding the proposed package insert:

1. Under **PRECAUTIONS, Pregnancy**, PRAVACHOL, the text reads, Pregnancy Category X, see **CONTRAINDICATIONS.** It then goes on to provide the same information that is provided in the referenced **CONTRAINDICATIONS** section. The additional (redundant) text should be deleted from the **Pregnancy** subsection (see 21CFR201.57).

2. Under **CONTRAINDICATIONS**, PRAVACHOL, the reference to the **PRECAUTIONS, Pregnancy**, PRAVACHOL subsection should be deleted as there is no *additional* information in that subsection.

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4. Under **PRECAUTIONS, Carcinogenesis, Mutagenesis, Impairment of Fertility**, BUFFERIN, the parenthetical reference to the Pregnancy subsection is unnecessary and should be deleted.

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[1] Although Bufferin is not currently marketed in an 81 mg strength, the sponsor notes that "the 81 mg tablet will have identical composition (same drug/excipient ratio) to the 325 mg tablet and will differ only in tablet weight."

5. *The **ANIMAL TOXICOLOGY** header and text which have been placed under **PRECAUTIONS**,* **Carcinogenesis, Mutagenesis, Impairment of Fertility**, BUFFERIN, should be deleted. Most of the information is provided elsewhere in the package insert or is not useful. The statement regarding renal papillary necrosis and decreased urinary concentrating ability in rodents should be moved to a **PRECAUTIONS** subsection titled **Renal Toxicity**, BUFFERIN, to be placed after the **PRECAUTIONS** subsection, **CNS Toxicity**, PRAVACHOL.

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NDA 21387.doc
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/s/

Charles Resnick
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