any reports of an interaction between selegiline and sympathomimetic amines. The agency invites any interested person with knowledge of such an interaction having occurred to provide that information to the agency.

Because of the relative nature of the selectivity of selegiline, the lack of knowledge about the precise mechanism of the MAOI-sympathomimetic amine interaction, and a lack of data on the effects of MAO B inhibitors on the pharmacokinetics and dynamics of sympathomimetic amines, the agency believes there is a need to consider whether the drug interaction precaution statement should be expanded to include MAO B drugs such as selegiline. If the warning statement were to be expanded, it would be revised to read: "Do not use this product if you are taking a prescription drug containing a monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric or emotional conditions, or Parkinson's disease), without first consulting your doctor. If you are uncertain whether your prescription drug contains an MAOI, consult a health professional before taking this product."

The agency is inviting specific additional comments on whether, from a public health perspective, it would be appropriate to expand the bronchodilator drug interaction precaution as indicated above. In order to fully consider this aspect of the proposed labeling, the agency is extending the comment period for this notice of proposed rulemaking an additional 60 days.

Interested persons may, on or before October 5, 1992, submit to the Dockets Management Branch (address above) written comments on the possible expansion of the drug interaction precaution statement proposed for OTC bronchodilator drug products containing sympathomimetic amines. Three copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: July 29, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 92-18618 Filed 8-5-92; 8:45 a.m.]

BILLING CODE 4160-01-F

21 CFR Part 341

[Docket No. 76N-052N]

RIN 0905-AA06

Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Proposed Amendment of Tentative Final Monograph for OTC Nasal Decongestant Drug Products; Request for Additional Comments; Extension of Comment Period

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of proposed rulemaking; request for additional comment; extension of comment period.

SUMMARY: The Food and Drug Administration (FDA) is extending to October 5, 1992, the comment period for the notice of proposed rulemaking amending the tentative final monograph for over-the-counter (OTC) nasal decongestant drug products to modify the drug interaction precaution statement proposed in the labeling of OTC oral nasal decongestant drug products containing sympathomimetic amines (57 FR 27658, June 19, 1992). This action is being taken because the agency would like additional comments on a possible addition to the proposed drug interaction precaution statement. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments by October 5, 1992.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 19, 1992 (57 FR 27658), FDA published a notice of proposed rulemaking to amend the tentative final monograph for OTC nasal decongestant drug products to include the following drug interaction precaution statement for OTC oral nasal decongestant drug products containing sympathomimetic amines to read: "Do not take this product if you are taking a prescription drug containing a monoamine oxidase inhibitor (MAOI) (certain drugs for depression or psychiatric or emotional conditions), without first consulting your doctor. If you are uncertain whether your prescription drug contains an MAOI, consult a health professional before taking this product." The closing date for comments on the proposal is August 18, 1992. In the **Federal Register** of July 30, 1992 (57 FR 33663), FDA published a correction that changes the wording of the first sentence of the statement to read, "*Drug interaction precaution.* Do not use this product if you are taking a prescription drug containing a monoamine oxidase inhibitor * * *."

In the notice of proposed rulemaking, the agency discussed the history of the drug interaction precaution statement and the reasons for revising its wording. The agency mentioned that there has been a resurgence in the use of MAOI drugs after a period of decline in the 1970's, and there is evidence that MAOI drugs are also being used to treat a wider variety of conditions, such as bulimia, panic disorders, phobic disorders, anxiety, and obsessive compulsive disorder (57 FR 27658). However, the use of MAOI drugs in hypertension has essentially ceased.

There are at least two types of monoamine oxidase (MAO) enzymes: the A form and B form. The two forms are characterized by differential substrate profiles, sensitivity to inhibition by clorgeline, and anatomical locations. MAO A preferentially deaminates norepinephrine and serotonin (5-hydroxytryptamine [5-HT]) and is sensitive to inhibition by clorgeline. MAO A is the unique form located in intestinal mucosa and placenta and predominates in peripheral nerve terminals. In contrast, MAO B preferentially deaminates phenethylamine and benzylamine, is inhibited by selegiline but not clorgeline, and is the unique form located in platelets. Both MAO A and MAO B are found in approximately equal proportions in the liver and brain.

The MAOI drugs marketed in the United States for psychiatric indications are nonspecific. They irreversibly inhibit both MAO A and MAO B. Selegiline is a relatively selective MAO B inhibitor indicated for use in Parkinson's disease treatment. At doses greater than 10 milligrams per day and, perhaps, at lower doses in some people, selegiline's selectivity decreases. Other, apparently more specific, MAO B inhibitors are now under development.

The agency did not address selegiline or MAO B inhibitors in the earlier proposal. The agency has not received any reports of an interaction between selegiline and sympathomimetic amines. The agency invites any interested person with knowledge of such an

interaction having occurred to provide that information to the agency.

Because of the relative nature of the selectivity of selegiline, the lack of knowledge about the precise mechanism of the MAOI-sympathomimetic amine drug interaction, and a lack of data on the effects of MAO B inhibitors on the pharmacokinetics and dynamics of sympathomimetic amine drugs, the agency believes there is a need to consider whether the drug interaction precaution statement should be expanded to include MAO B drugs such as selegiline. If the warning statement were to be expanded, it would be revised to read: "Do not use this product if you are taking a prescription drug containing a monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric or emotional conditions, or Parkinson's disease), without first consulting your doctor. If you are uncertain whether your prescription drug contains an MAOI, consult a health professional before taking this product."

The agency is inviting specific additional comments on whether, from a public health perspective, it would be appropriate to expand the nasal decongestant drug interaction precaution as indicated above. In order to fully consider this aspect of the proposed labeling, the agency is extending the comment period for this notice of proposed rulemaking an additional 60 days.

Interested persons may, on or before October 5, 1992, submit to the Dockets Management Branch (address above) written comments on the possible expansion of the drug interaction precaution statement proposed for OTC nasal decongestant drug products containing sympathomimetic amines. Three copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: July 29, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy.

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21 CFR Part 341

[Docket No. 90N-0420]

RIN 0905-AA06

Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Proposed Amendment of Final Monograph for OTC Antitussive Drug Products; Request for Additional Comments; Extension of Comment Period

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of proposed rulemaking; request for additional comment; extension of comment period.

SUMMARY: The Food and Drug Administration (FDA) is extending to October 5, 1992, the comment period for the notice of proposed rulemaking amending the final monograph for over-the-counter (OTC) antitussive drug products to require a drug interaction precaution statement in the labeling of OTC antitussive (relieves cough) drug products containing dextromethorphan or dextromethorphan hydrobromide (57 FR 27666, June 19, 1992). This action is being taken because the agency would like additional comments on a possible addition to the proposed drug interaction precaution statement. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments by October 5, 1992.

ADDRESSES: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 19, 1992 (57 FR 27666), FDA published a notice of proposed rulemaking to amend the final monograph for OTC antitussive drug products to include the following drug interaction precaution statement for OTC antitussive drug products containing dextromethorphan or dextromethorphan hydrobromide: "Do not use this product if you are taking a prescription drug containing a monoamine oxidase inhibitor (MAOI) (certain drugs for depression or psychiatric or emotional conditions), without first consulting your doctor. If you are uncertain whether your prescription drug contains an MAOI, consult a health professional before taking this product." The closing date for comments on the proposal is August 18, 1992.

In the notice of proposed rulemaking, the agency discussed reports of adverse reactions, including fatalities, following the ingestion of prescription MAOI drugs and OTC drug products containing the ingredient dextromethorphan or dextromethorphan hydrobromide (referred to generally as dextromethorphan). The agency mentioned that there has been a resurgence in the use of MAOI drugs after a period of decline in the 1970's, and there is evidence that MAOI drugs are also being used to treat a wider variety of conditions, such as bulimia, panic disorders, phobic disorders, anxiety, and obsessive compulsive disorder (57 FR 27666 at 27668). However, the use of MAOI drugs in hypertension has essentially ceased.

There are at least two types of monoamine oxidase (MAO) enzymes: the A form and B form. The two forms are characterized by differential substrate profiles, sensitivity to inhibition by clorgeline, and anatomical locations. MAO A preferentially deaminates norepinephrine and serotonin (5-hydroxytryptamine [5-HT]) and is sensitive to inhibition by clorgeline. MAO A is the unique form located in intestinal mucosa and placenta and predominates in peripheral nerve terminals. In contrast, MAO B preferentially deaminates phenethylamine and benzylamine, is inhibited by selegiline but not clorgeline, and is the unique form located in platelets. Both MAO A and MAO B are found in approximately equal proportions in the liver and brain.

The MAOI drugs marketed in the United States for psychiatric indications are nonspecific. They irreversibly inhibit both MAO A and MAO B. Selegiline is a relatively selective MAO B inhibitor indicated for use in Parkinson's disease treatment. At doses greater than 10 milligrams per day and, perhaps, at lower doses in some people, selegiline's selectivity decreases. Other, apparently more specific, MAO B inhibitors are now under development.

The agency did not address selegiline or MAO B inhibitors in the earlier proposal. The agency has not received any reports of an interaction between selegiline and dextromethorphan or dextromethorphan hydrobromide. The agency invites any interested person with knowledge of such an interaction having occurred to provide that information to the agency.