• Webform at the Federal eRulemaking Portal: *www.regulations.gov*. Follow the instructions at that site for submitting comments.

FOR FURTHER INFORMATION CONTACT: Meggan Engelke-Ros or Susan S. Beresford, 301–427–2202.

SUPPLEMENTARY INFORMATION: As announced in the **Federal Register** on October 12, 2004 (69 FR 60569), NOAA is proposing revisions to its Civil Procedures which govern the Agency's administrative proceedings for the assessment of civil penalties; suspension, revocation, modification, or denial of permits; issuance and use of written warnings; and release or forfeiture of seized property. The comment period for the proposed rule closed on December 13, 2004. While NOAA received comments expressing opinions about whether, and in what way, its Civil Procedures should be revised, NOAA was also asked to extend the comment period beyond the original 60 days. NOAA has reopened the comment period to provide the public an additional opportunity to comment on the proposed revisions. The agency believes these additional comments will aid in the evaluation of the proposed revisions. Comments received between December 13, 2004, and the publication date of this document will be given full consideration by NOAA.

Background

In October 2004, NOAA proposed revisions (69 FR 60569) to the civil procedure rules that apply to its administrative proceedings under 15 CFR part 904. Part 904 has been largely unchanged since 1987 and the proposed changes were intended to: (1) conform the civil procedure rules to changes in applicable Federal laws and regulations; (2) improve efficiency and fairness of administrative proceedings; (3) clarify any ambiguities or inconsistencies in the existing civil procedure rules; (4) eliminate redundant language and correct language errors; and (5) conform the civil procedure rules to current Agency practice.

NOAA invites comments on all aspects of the revisions proposed to part 904 from all interested parties. Information on the time period for submission of comments and directions for their submission may be found in the DATES and ADDRESSES section of this document.

It has been determined that this rule is not a ''significant regulatory action'' under the terms of Executive Order 12866 and is therefore not subject to OMB review.

Authority: 16 U.S.C. 1801–1882; 16 U.S.C. 1531–1543; 16 U.S.C. 1361–1407; 16 U.S.C. 3371–3378; 16 U.S.C. 1431–1439; 16 U.S.C. 773–773k; 16 U.S.C. 951–961; 16 U.S.C. 1021–1032; 16 U.S.C. 3631–3644; 42 U.S.C. 9101 *et seq.*; 30 U.S.C. 1401 *et seq.*; 16 U.S.C. 971–971k; 16 U.S.C. 781 *et seq.*; 16 U.S.C. 2401–2413; 16 U.S.C. 2431–2444; 16 U.S.C. 972–972h; 16 U.S.C. 916–916l; 16 U.S.C. 1151–1175; 16 U.S.C. 3601–3608; 16 U.S.C. 1851 note; 15 U.S.C. 4201 *et seq.*; Pub. L. 102–587; 106 Stat. 5039.

Dated: December 29, 2004.

Jane H. Chalmers,

Acting General Counsel, National Oceanic and Atmospheric Administration.

[FR Doc. 04–28751 Filed 12–30–04; 3:39 pm]

BILLING CODE 3510–12–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 357

[Docket No. 1982N–0166]

RIN 0910–AF51

Orally Administered Drug Products for Relief of Symptoms Associated With Overindulgence in Food and Drink for Over-the-Counter Human Use; Proposed Amendment of the Tentative Final Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend the tentative final monograph (TFM) for over-the-counter (OTC) orally administered drug products for relief of symptoms associated with overindulgence in food and drink to include an additional use for products that contain bismuth subsalicylate as an active ingredient labeled for the relief of symptoms of upset stomach due to overindulgence resulting from food and drink. This proposal is part of FDA's ongoing review of OTC drug products.

DATES: Submit written or electronic comments by April 5, 2005. Please see section X of this document for the proposed effective date of any final rule that may publish based on this proposal.

ADDRESSES: You may submit comments, identified by Docket No. 1982N–0166 or RIN 0910–AF51, by any of the following methods:

• Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.

• Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow the instructions for submitting comments on the agency Web site.

• E-mail: *fdadockets@oc.fda.gov*. Include Docket No. 1982N–0166 or RIN 0910–AF51 in the subject line of your e-mail message.

• FAX: 301–827–6870.

• Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]: Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the agency name and Docket No. or Regulatory Information Number (RIN) for this rulemaking. All comments received will be posted without change to *http://www.fda.gov/dockets/ecomments*, including any personal information provided. For detailed instructions on submitting comments and additional information on the rulemaking process, see the ''Request for Comments'' heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://www.fda.gov/dockets/ecomments*and/or the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Gerald M. Rachanow, Center for Drug Evaluation and Research (HFD–560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2307.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of October 1, 1982 (47 FR 43540), FDA published an advance notice of proposed rulemaking to establish a monograph for OTC orally administered drug products for relief of symptoms associated with overindulgence in alcohol and food, together with the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in these drug products (§ 330.10(a)(6) (21 CFR 330.10(a)(6))).

In the **Federal Register** of December 24, 1991 (56 FR 66742), FDA published the proposed rule (in the form of a TFM) for OTC orally administered drug products for relief of symptoms associated with overindulgence in food and drink. In the **Federal Register** of May 5, 1993 (58 FR 26886), FDA proposed to amend the overindulgence TFM to include a Reye's syndrome warning for OTC drug products containing bismuth subsalicylate. In the

Federal Register of April 17, 2003 (68 FR 18861), FDA published a final rule to revise the Reye's syndrome warning (§ 201.314(h) (21 CFR 201.314(h))) to include OTC drug products containing nonaspirin salicylates (e.g., bismuth subsalicylate) as active ingredients. FDA stated that there was no need to address this warning in a separate rule for overindulgence drug products containing bismuth subsalicylate (68 FR 18861 at 18862). Thus, the April 17, 2003, final rule completed the May 5, 1993, proposed rule. Products containing bismuth subsalicylate as an active ingredient must contain the required Reye's syndrome warning statement as of April 19, 2004, except that products with annual sales less than $25,000 have until April 18, 2005, to be in compliance.

In the **Federal Register** of March 17, 1999 (64 FR 13254), FDA established a standardized format and content for the labeling of all OTC drug products (see § 201.66). The labeling in the TFM and the labeling in this amendment are not in that format. However, the labeling in the final monograph (FM) will incorporate the standardized labeling format and content. In response to the TFM, FDA received a number of comments and is addressing part of one comment in this document. The remaining comments will be addressed in the final rule. All ''OTC Volumes'' cited throughout this document refer to information on public display in the Division of Dockets Management (see **ADDRESSES**).

II. The Comment's Recommendation, Arguments, and Data

One comment recommended that FDA include combination upset stomach/antiflatulent (antigas) drug products containing bismuth subsalicylate and simethicone in the overindulgence monograph for the relief of upset stomach and gas due to overindulgence in food and drink. The comment provided the following arguments and data to support its recommendation.

- FDA's ''General Guidelines for OTC Drug Combination Products, September 1978'' (Ref. 1) provide that Category I active ingredients from different therapeutic categories may be combined to treat different symptoms concurrently if each ingredient is present within its established safe and effective dosage range, and the combination meets the OTC drug combination policy in all other respects. FDA's OTC drug combination regulations (§ 330.10(a)(4)(iv)) provide that an OTC drug may combine two or more safe and effective active ingredients and may be generally recognized as safe and effective when each active ingredient makes a contribution to the claimed effect(s); when combining of the active ingredients does not decrease the safety or effectiveness of any of the individual active ingredients; and when the combination, when used under adequate directions for use and warnings against unsafe use, provides rational concurrent therapy for a significant proportion of the target population. A combination drug product containing bismuth subsalicylate and simethicone would combine two Category I active ingredients as specified in these Guidelines and meet the requirements of this regulation.
- FDA proposed bismuth subsalicylate as safe and effective for the relief of symptoms of upset stomach associated with overindulgence in food and drink in the TFM, and simethicone is included in the antiflatulent monograph (21 CFR part 332). Bismuth subsalicylate acts in the stomach to relieve upset stomach/indigestion symptoms such as nausea, heartburn, and fullness, while simethicone acts in the stomach to break up gas bubbles resulting from overindulgence in food and drink. Together, these active ingredients will provide relief from upset stomach symptoms occurring in the presence of gas.
- Combining the active ingredients does not decrease the safety and effectiveness of either ingredient. The comment cited data to support that (1) Bismuth subsalicylate does not decrease the foam-reducing capacity of simethicone (Ref. 2), (2) serum salicylate bioavailability of a combination of bismuth subsalicylate-simethicone was equivalent to bismuth subsalicylate alone in dogs (Ref. 3), and (3) the combination and bismuth subsalicylate alone in rats provided equivalent stomach protection against alcohol (Ref. 4).
- The combination provides rational concurrent therapy for a significant proportion of the target population. The comment noted a consumer study of 285 subjects suffering from upset stomach due to overindulgence in which 56 percent of the subjects reported gas as one of their symptoms (Ref. 5). The comment mentioned another consumer study of 159 adults who reported having gas concurrently with symptoms for which bismuth subsalicylate has been shown to be effective (Ref. 6). The percent of adults reporting gas with each symptom included: Fullness/bloating (57), upset stomach (55), indigestion (44), and heartburn (24).
- Antacid-simethicone combination products were included in the antacid monograph (21 CFR part 331) and the antiflatulent monograph without any supporting clinical data. FDA's determination to allow this combination was based on a reasonable expectation that simethicone will be effective if used in combination with an antacid drug product (38 FR 31260 at 31266, November 12, 1973). Further, FDA has proposed that any antacid covered by the antacid monograph may be labeled ''for the relief of * * * upset stomach associated with * * * overindulgence in food and drink'' (56 FR 66754 at 66756, December 24, 1991). FDA did not review any clinical data to support the indication of upset stomach and gas due to overindulgence in food and drink.

III. FDA's Evaluation of the Comment's Recommendation

FDA has evaluated the comment's recommendation and reconsidered the Panel's review of bismuth subsalicylate for the relief of symptoms of upset stomach associated with overindulgence in food and drink. The Panel stated that upset stomach that occurs as a result of overindulgence in food and drink consists of a group of symptoms that includes heartburn, fullness, and nausea (47 FR 43540 at 43543 and 43545). One of the indications statements that the Panel recommended for products containing bismuth subsalicylate included these symptoms: ''For the relief of upset stomach associated with'' (select one or more of the following: ''nausea,'' ''heartburn,'' and ''fullness'') ''due to overindulgence in the combination of food and drink.'' (See 47 FR 43540 at 43550 and 43558.) FDA proposed this indication statement without the words ''the combination of'' in § 357.950(b)(2) of the TFM (see 56 FR 66742 at 66751).

The Panel discussed the consumer study of 285 subjects (Ref. 5) (47 FR 43540 at 43545), cited by the comment, and noted that 96 percent of the subjects had at least one of the symptoms of ''gas (fullness), heartburn (or acid indigestion), or nausea'' and that 56 percent [the highest percentage] reported gas as one of their symptoms. The Panel cited studies by Newsom (Ref. 7) and by Berkowitz (Ref. 8) (47 FR 43540 at 43548 to 43549) to support the effectiveness of bismuth subsalicylate for treating upset stomach due to overindulgence. The Newsom study was subsequently published in the *Archives of Internal Medicine* (Ref. 9).

Newsom conducted a randomized, placebo-controlled, double-blind, multiple-crossover study (Refs. 7 and 9) to evaluate the effectiveness of bismuth

subsalicylate to relieve symptoms in subjects with a history of episodic, acute (having a short and relatively severe course) indigestion. The study involved 48 adult subjects 18 to 49 years old (20 men, 28 women). Two additional subjects began the study but were later excluded by the investigator because of abnormal laboratory values. The study medication consisted of either 16.7 milligrams per milliliter (mg/mL) of bismuth subsalicylate suspended in the vehicle or a placebo of vehicle only. The two preparations were similar in appearance, flavor, and viscosity. Each subject received three bottles of each formulation with a computer-generated random sequence of use for treating six episodes over a 7-month period. The subjects were instructed to take the study medication only when they experienced two or more of the symptoms and to take 30 mL every 30 minutes as needed for a total of eight doses (up to 240 minutes). Subjects recorded specific symptoms and the time they first occurred, rating symptom severity on a 10-point scale 15 and 30 minutes after each dose. Subjects reported the time when relief occurred. After six episodes, each subject evaluated each preparation three times.

Newsom defined indigestion or acute gastrointestinal discomfort as a symptom complex consisting of two or more of the following symptoms occurring during or after ingestion of food: Nausea, heartburn, upper-abdominal pain, flatulence (gas) and eructation (belching), sense of fullness, or a feeling of abdominal distention. *Stedman's Medical Dictionary* (Ref. 10) defines indigestion as a nonspecific term for a variety of symptoms resulting from a failure of proper digestion and absorption of food in the alimentary tract [relating to the organs of digestion]. FDA notes that the investigator's definition of indigestion or acute gastrointestinal discomfort is consistent with the Stedman's definition in that the dictionary's term is nonspecific and the investigator's symptoms relate to the digestive system.

The 48 test subjects had no significant differences in reported symptoms or identified causes in the six individual episodes of symptoms. Eating specific foods was the most commonly identified cause of symptoms, followed by overeating. The overall relief of symptoms showed more episodes treated with bismuth subsalicylate were relieved (132/144) than were episodes treated with placebo (121/144). However, the difference between the two groups was not statistically significant ($0.05<p<0.10$). However, when time to relief was evaluated in 30-minute intervals, the episodes treated with bismuth subsalicylate were relieved in 90 minutes (median) compared to 120 minutes (median) for episodes treated with placebo. The difference was statistically significant ($p<0.01$). In addition, the differences in time to relief were significant at the time intervals of 31 to 60, 61 to 90, and 91 to 120 minutes ($p<0.01$). Beginning at 30 to 45 minutes post-medication, a statistically significant more rapid decrease in severity of nausea, heartburn, flatulence and eructation, and sense of fullness occurred in the subjects receiving bismuth subsalicylate compared to subjects receiving placebo. The feeling of abdominal distension was less severe at 90 minutes with bismuth subsalicylate, but the severity of upper abdominal pain was no different with either treatment. Comparing the time to relief shows that bismuth subsalicylate provided significantly faster relief than placebo for nausea, heartburn, flatulence and eructation, and sense of fullness. FDA concludes that this study supports that bismuth subsalicylate relieves the symptoms of flatulence and eructation, which are symptoms from gas. The study also supports that bismuth subsalicylate relieves the sense of fullness, which might be related to gas.

Berkowitz conducted a randomized, placebo-controlled, double-blind study (Ref. 8) to evaluate the effectiveness of bismuth subsalicylate to relieve gastrointestinal symptoms, commonly termed as ''upset stomach,'' from consumption of food and drink. One hundred thirty two healthy adult subjects fasted for 6 hours and then were provided unlimited quantities of provocative food and drink. The subjects were provided a diary to record eight symptoms, degree of discomfort (none, mild, moderate, severe), and the time of occurrence. The symptoms were:

- stomach queasiness/nausea
- heartburn
- sense of fullness/bloated feeling
- belching
- bitter or acid taste in mouth
- passing gas/wind
- stomach pain/cramps
- other symptoms

The subjects were instructed to take 30 mL of the test medication when symptoms first occurred and to repeat the dose every 30 to 60 minutes, if needed, up to eight doses. The test medication (bismuth subsalicylate) and the placebo were prepared as white, opaque suspensions identical in flavor and viscosity. However, Berkowitz did not mention the concentration of the bismuth subsalicylate preparation. Subjects recorded the time the dose was taken and the degree of relief obtained (none, poor, good, excellent).

Ninety-one of the 132 subjects developed symptoms that required medication, with 43 taking bismuth subsalicylate and 48 taking placebo. Comparison of the two groups showed no significant demographic or baseline differences. The number of subjects and the percent of 91 total subjects reporting the symptoms were as follows:

- stomach queasiness/nausea - 50 (55%)
- heartburn - 48 (53%)
- sense of fullness/bloated feeling - 66 (73%)
- belching - 50 (55%)
- bitter or acid taste in mouth - 18 (20%)
- passing gas/wind - 30 (33%)
- stomach pain/cramps - 17 (19%)

The number of symptoms reported is greater than the number of subjects because subjects reported more than one symptom. Berkowitz performed a statistical analysis of the four relief categories for each symptom and for overall relief. Berkowitz found that bismuth subsalicylate was significantly more effective than placebo for each category except bitter/acid taste. When the analysis was done using (1) Two relief categories (none and poor counted as failure, and good and excellent counted as success) and (2) time to good or excellent relief for each symptom, Berkowitz found that bismuth subsalicylate was significantly more effective and provided significantly faster relief than placebo for relief of nausea, fullness, heartburn, belching, and overall relief. There was no statistical difference in relief of stomach pain/cramps, passing gas, and bitter/acid taste. FDA finds that, although all data are not clearly shown in this study, the results support that bismuth subsalicylate is effective in relieving nausea, heartburn, fullness, and belching. FDA notes that the medical definitions of flatulence, eructation, and bloating are defined using the word gas. While ''fullness'' is not defined in *Stedman's Medical Dictionary* (Ref. 10) or in *Dorland's Illustrated Medical Dictionary* (Ref. 11), Berkowitz combined the term ''fullness'' with the term ''bloating,'' which refers to abdominal distention from swallowing air or from intestinal gas, and showed that bismuth subsalicylate relieved fullness and bloating.

FDA notes that, in evaluating the consumer study of 285 subjects (Ref. 5) (47 FR 43540 at 43545), the Panel noted that 96 percent of the subjects had at least one of the symptoms of gas (fullness), heartburn (or acid indigestion), or nausea, and that 56

percent [the highest percentage] reported gas as one of their symptoms. Nonetheless, the Panel used the term ''fullness'' (and not ''gas'') in its proposed indication for overindulgence drug products containing bismuth subsalicylate (47 FR 43540 at 43558). FDA believes that the Panel also found that bismuth subsalicylate relieves gas due to overindulgence in food and drink, but chose to use the word ''fullness'' instead in its recommended indications statement. FDA also points out that its current indications statement for OTC antiflatulent drug products containing simethicone in § 332.30(b)(2) states: ''(Select one of the following: 'Alleviates' or 'Relieves') (select one or more of the following: 'bloating,' 'pressure,' 'fullness,' or 'stuffed feeling') 'commonly referred to as gas'.'' Thus, FDA already acknowledges that the term ''fullness'' encompasses the term ''gas.''

As the comment noted, the combination of bismuth subsalicylate and simethicone is subject to FDA's combination drug policy (see section II of this document). However, FDA notes that a bismuth subsalicylate-simethicone combination is different than the antacid-simethicone combination that the comment discussed. Simethicone is a monograph ingredient (see § 332.10) for antiflatulent use (to relieve fullness and bloating commonly referred to as gas). Bismuth subsalicylate is not included in the antacid monograph but based on the information and analysis in this document has an antigas (antiflatulent) effect when relieving symptoms of overindulgence in food and drink. This analysis and finding are new information that the comment did not have when it proposed a bismuth subsalicylate-simethicone combination product.

FDA's regulation in § 330.10(a)(4) sets forth the standard for determining whether a combination drug product may be generally recognized as safe and effective and not misbranded. Section 330.10(a)(4)(iv) states that ''an OTC drug may combine two or more safe and effective active ingredients and may be generally recognized as safe and effective when each active ingredient makes a contribution to the claimed effect(s) * * *.'' FDA's ''General Guidelines for OTC Drug Combination Products, September 1978'' [''Combination Product Guidelines''] (Ref. 1) state that Category I active ingredients from the same therapeutic category [''antiflatulent'' in this case] that have the same mechanism of action may be combined in selected circumstances to treat the same symptoms if:

- The combination meets the OTC combination policy in all respects;
- the combination offers some advantage over the active ingredients used alone; and
- the combination is, on a benefit-risk basis, equal to or better than each of the active ingredients used alone at its therapeutic dose.

The ''Combination Product Guidelines'' (Ref. 1) list similar factors in assessing combination drug products with active ingredients from the same therapeutic category that have different mechanisms of action.

FDA does not have any data on the antigas mechanism of action of bismuth subsalicylate to determine if it is the same or different from that of simethicone. FDA also has not received any data to date comparing the antigas effectiveness of a combination of the two ingredients versus either individual ingredient. Further, FDA is not aware of any combination product containing bismuth subsalicylate and simethicone having been marketed. Therefore, FDA needs data from clinical studies showing that the combination of bismuth subsalicylate and simethicone is equal to or better than [offers some advantage over] each of the individual active ingredients used alone at its therapeutic dose for this antigas use. FDA recommends that anyone interested in conducting such studies submit a protocol and meet with the agency before starting the studies. FDA will evaluate the other data (Refs. 2, 3, and 4) that the comment provided to support this combination product when the clinical effectiveness studies are submitted to FDA.

IV. FDA's Proposed Amendment of the Tentative Final Monograph

Based on the Newsom (Refs. 7 and 9) and Berkowitz (Ref. 8) studies, FDA has tentatively determined that bismuth subsalicylate is safe and effective for OTC use for the relief of upset stomach associated with belching and gas due to overindulgence in food and drink. FDA proposes to amend the definition of ''upset stomach due to overindulgence in food and drink'' proposed in § 357.903 to add the symptoms ''belching'' and ''gas'' and to amend the indications statement for bismuth subsalicylate proposed in § 357.950(b)(2) to add ''belching'' and ''gas'' as two additional symptoms that manufacturers may select to include in the labeling of these products.

V. Analysis of Impacts

FDA has examined the impacts of this proposed rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1501 *et seq.*). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million (adjusted annually for inflation) in any one year.

FDA believes that this proposed rule is consistent with the principles set out in Executive Order 12866 and in these two statutes. The proposed rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order. The Unfunded Mandates Reform Act of 1995 does not require FDA to prepare a statement of costs and benefits for this proposed rule, because the proposed rule is not expected to result in any 1-year expenditure that would exceed $100 million adjusted for inflation. The current inflation adjusted statutory threshold is about $110 million.

The purpose of this proposed rule is to expand an indications statement for OTC overindulgence drug products that contain bismuth subsalicylate as their active ingredient. The proposal provides manufacturers the option of including two additional symptoms in their product's indications statement. As this additional labeling is optional, manufacturers may elect to implement it whenever they revise product labeling or may elect not to include the additional information at all. FDA is unable to state exactly how many bismuth subsalicylate products have an overindulgence claim because these products may be marketed with other claims (e.g., for diarrhea) and not have an overindulgence claim. FDA's Drug Listing System (DLS) identifies 334 OTC drug products that contain bismuth subsalicylate and are marketed for use

as an antidiarrheal. Some of these products may also have a claim for overindulgence or may want to include a claim for overindulgence. Because these products could be marketed with an overindulgence claim, FDA is counting all such products as potentially affected by this proposed rule. However, because any relabeling resulting from this proposed rule is completely voluntary and can be done when manufacturers are ordering new product labeling, FDA considers any costs resulting from this proposed rule to be negligible. FDA recognizes that frequent labeling redesigns are a recognized cost of doing business in the OTC drug industry. Manufacturers that make voluntary market-driven changes to their labeling can usually do so at a nominal cost. FDA recognizes benefits to both manufacturers and consumers from this proposed labeling change. Manufacturers will have two additional uses for these products to promote to consumers, and consumers will be able to use a single product instead of two products (one for overindulgence and one for gas) to relieve their symptoms resulting from overindulgence in food and drink. FDA did not consider other labeling alternatives.

This analysis shows that FDA has considered the burden to small entities. Therefore, FDA certifies that this proposed rule will not have a significant economic impact on a substantial number of small entities. No further analysis is required under the Regulatory Flexibility Act (5 U.S.C. 605(b)).

VI. Paperwork Reduction Act of 1995

FDA tentatively concludes that the labeling proposed in this document is not subject to review by the Office of Management and Budget because they do not constitute a ''collection of information'' under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*). Rather, the proposed labeling is a ''public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public'' (5 CFR 1320.3(c)(2)).

VII. Environmental Impact

FDA has determined under 21 CFR 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, FDA tentatively concludes that the proposed rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement has not been prepared.

IX. Request for Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Three copies of all written comments are to be submitted. Individuals submitting written comments or anyone submitting electronic comments 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 Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

X. Proposed Effective Date

FDA is proposing that any final rule that may be issued based on this proposal be included in the future FM for OTC orally administered drug products for relief of symptoms associated with overindulgence in food and drink and have the same effective date as that FM.

XI. References

The following references are on display in the Division of Dockets Management (see **ADDRESSES**), under Docket No. 1982N–0166 unless otherwise noted, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. FDA, ''General Guidelines for OTC Drug Combination Products, September 1978,'' Division of Dockets Management, Docket No. 1978D–0322.

2. The Procter & Gamble Co., ''*In-vitro* Foam Reducing Capacity Test: Pepto-Bismol With Simethicone,'' in C12.

3. Lukacovic, M. F. and K. J. Watters, ''Dog Bioavailability Study With Pentagastrin—Pepto-Bismol With Simethicone, PBDB #14,'' The Procter & Gamble Co., in C12, 1992.

4. Lukacovic, M. F. and K. J. Watters, ''Rat Gastric Lesion Study–Pepto-Bismol With Simethicone. EtOH Study—ANTR #53,'' The Procter & Gamble Co., in C12, 1991.

5. Comment 31–11370, Division of Dockets Management, Docket No. 1978N–0263.

6. ''Study #PD 0292–07,'' The Procter & Gamble Co., in C12.

7. Newsom, J. H., ''Evaluation of Bismuth Subsalicylate in Relieving Symptoms of Indigestion,'' OTC Vol. 170208 (pp. 15–17).

8. Berkowitz, J. M., ''Bismuth Subsalicylate in Excessive Alcohol/Food Intake,'' OTC Vol. 170208 (pp. 11–15).

9. Hailey, F. J. and J. H. Newsom, ''Evaluation of Bismuth Subsalicylate in Relieving Symptoms of Indigestion,'' *Archives of Internal Medicine*, 144:269–272, 1984.

10. *Stedman's Medical Dictionary*, 25th ed., Williams & Wilkins, Baltimore, MD, s.v. ''indigestion,'' 1990.

11. *Dorland's Illustrated Medical Dictionary*, 28th ed., W. B. Saunders Co., Philadelphia, PA, 1994.

List of Subjects in 21 CFR Part 357

Labeling, Over-the-counter drugs, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 357, as proposed in the **Federal Register** of December 24, 1991 (56 FR 66742), be amended as follows:

PART 357—MISCELLANEOUS INTERNAL DRUG PRODUCTS FOR OVER–THE–COUNTER HUMAN USE

1. The authority citation for 21 CFR part 357 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

2. Section 357.903 is amended by revising paragraph (a) to read as follows:

§ 357.903 Definitions.

* * * * *

(a) *Upset stomach due to overindulgence in food and drink.* A condition that occurs as a result of overindulgence in food and drink and consists of a group of symptoms that includes heartburn, nausea, fullness, belching, and gas.

* * * * *

3. Section 357.950 is amended by revising paragraph (b)(2) to read as follows:

§ 357.950 Labeling of drug products for the relief of symptoms of upset stomach due to overindulgence in food and drink.

* * * * *

(b) * * *

(2) ''For the relief of upset stomach associated with'' (select one or more of the following: ''nausea,'' ''heartburn,'' ''fullness,'' ''belching,'' and ''gas'') ''due to overindulgence in food and drink.''

* * * * *

Dated: December 15, 2004.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[REG–117969–00]

RIN 1545–BD76

Statutory Mergers and Consolidations

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Amendment of previously proposed regulations and notice of public hearing.

SUMMARY: This document amends previously proposed regulations published in the **Federal Register** on January 24, 2003 (REG–126485–01, 2003–9 I.R.B. 542, 68 FR 3477) by cross-reference to temporary regulations. Those regulations define the term *statutory merger or consolidation* as that term is used in section 368(a)(1)(A). This notice of proposed rulemaking affects corporations engaging in mergers and consolidations and their shareholders. It is being issued concurrently with proposed regulations under sections 358, 367, and 884. (*See* REG–125628–01 in the proposed rulemaking section of this issue of the **Federal Register**).

DATES: Written and electronic comments and requests to speak and outlines of topics to be discussed at the public hearing scheduled for May 19, 2005, to be held in the IRS Auditorium (7th floor) must be received by April 28, 2005.

ADDRESSES: Send submissions to CC:PA:LPD:PR (REG–117969–00), Room 5203, Internal Revenue Service, POB 7604, Ben Franklin Station, Washington, DC 20044. Submissions may be hand delivered Monday through Friday between the hours of 8 a.m. and 4 p.m. to: CC:PA:LPD:PR (REG–117969–00), Courier's Desk, Internal Revenue Service, 1111 Constitution Avenue, NW., Washington, DC, or sent electronically, via the IRS Internet site at *http://www.irs.gov/regs* or via the Federal eRulemaking Portal at *http://www.regulations.gov* (IRS–REG–117969–00). The public hearing will be held in the IRS Auditorium (7th floor), Internal Revenue Building, 1111 Constitution Avenue, NW., Washington, DC.

FOR FURTHER INFORMATION CONTACT: Concerning the proposed regulations, Vincent Daly, (202) 622–7770; concerning submissions, the hearing, or placement on the building access list to attend the hearing, Robin Jones, (202) 622–7180 (not toll-free numbers).

SUPPLEMENTARY INFORMATION:

Background and Explanation of Provisions

Before 1934, the term *merger*, as used in the reorganization provisions, included statutory mergers as well as other combinations of corporate entities. In 1934, congress amended the definition of a reorganization to provide separately for *statutory mergers or consolidations* and for the other types of transactions previously included in the definition of a *merger*. There is no indication in the legislative history of the 1934 changes to the definition of reorganization that Congress intended to exclude transactions effected under foreign law.

In 1935, Treasury regulations interpreted the term *statutory merger* under the revised provision to mean a merger or consolidation effected pursuant to the corporation laws of a State or Territory or the District of Columbia. The requirement that the transaction be effected under domestic law remains in place, with minor variations. The Treasury Department and IRS believe that this interpretation is reasonable; nevertheless, the Treasury Department and IRS believe that a reexamination is warranted in light of the purposes of the statute and changes in domestic and foreign law since 1935.

The states have revised their laws to offer a greater variety of business entities and greater flexibility in effecting business combinations. Accordingly, the Treasury Department and IRS thought it advisable to define a merger or consolidation functionally, to supplement the reference to State law. Accordingly, the Treasury Department and IRS developed and proposed such a functional definition in 2003. See Notice of Proposed Rulemaking (REG–126485–01, 2003–9 I.R.B. 542, 68 FR 3477), cross-referencing temporary regulations (TD 9038, 2003–9, I.R.B. 524, 68 FR 3384) (January 24, 2003).

Many foreign jurisdictions now have merger or consolidation statutes that operate in material respects like those of the states, *i.e.*, all assets and liabilities move by operation of law. The Treasury Department and IRS believe that transactions affected pursuant to these statutes should be treated as reorganizations if they satisfy the functional criteria applicable to transactions under domestic statutes.

This document proposes a revised definition of a statutory merger or consolidation. The previously proposed definition of a statutory merger required that it be a transaction effected ''pursuant to the laws of the United States or a State or the District of Columbia.'' See REG–126485–01 (2003–9 I.R.B. 542, 68 FR 3477). The new proposed definition contained in this document replaces the quoted language with ''pursuant to the statute or statutes necessary to effect the merger or consolidation.'' This proposed change would allow a transaction effected pursuant to the statutes of a foreign jurisdiction or of a United States possession to qualify as a statutory merger or consolidation under section 368(a)(1)(A), provided it otherwise qualifies as a reorganization. The phrase *statute or statutes* is not intended to prevent transactions effected pursuant to legislation from qualifying as mergers or consolidations where such legislation is supplemented by administrative or case law.

This notice of proposed rulemaking also proposes to remove § 1.368–2(b)(1)(iii) of the previously proposed regulations. That section imposes limitations on the use of disregarded entities in statutory mergers or consolidations when certain entities are not organized under the laws of the United States or a State or the District of Columbia.

Although this document revises the terms of the proposed definition of a statutory merger or consolidation for purposes of section 368, the provisions of the temporary regulations will remain in effect until this proposal is incorporated in temporary or final regulations after notice and comment.

Section 1.368–2(b)(1)(B)(iv), *Examples 1* and *2* in the previously proposed regulations each specified that one of the parties to the transaction described in the example ''is not treated as owning any assets of an entity that is disregarded as an entity separate from its owner for Federal tax purposes.'' The results in those examples would be the same in each case whether or not a party to the transaction held such assets. See