

products be labeled to state the results they provide and the timeframe in which they occur. Therefore, the agency is including the following indication for kaolin in this final monograph: "Helps firm stools within 24 to 48 hours" (see section III of this document).

Kaolin is an adsorbent that can interfere with the gastrointestinal absorption of a number of oral medications, including some antibiotics, digitalis glycosides, and theophylline, resulting in decreased therapeutic effectiveness. The interaction might be avoided if kaolin is given at least 3 hours before or after taking any oral medication. Therefore, the agency is requiring a specific drug interaction precaution statement for products containing kaolin: "Ask a doctor or pharmacist before use if you are taking any other drugs. Try to use at least 3 hours before or after taking any other drugs."

The committees also noted that the available data did not address the safety and effectiveness of kaolin in children and recommended that the ingredient should not be administered to children under 12 years of age without the specific recommendations of a doctor. Further, the agency is concerned about use in children because they may have a greater potential for fluid loss and electrolyte imbalance due to diarrhea and antidiarrheal products that only improve stool consistency may mask the extent of fluid loss. Dehydration due to diarrhea in children can occur early in the disease process and may have serious consequences, such as circulatory collapse and renal failure (Ref. 32). Kaolin improves stool consistency in 24 to 48 hours. However, current information is insufficient to show whether it also reduces fluid and electrolyte loss. None of the studies demonstrated the effectiveness of kaolin in children under 12 years of age. As noted in the TFM (51 FR 16138 at 16145), one study on the use of kaolin and pectin in children 3 to 11 years old indicated some possible benefit for a greater number of formed stools and a smaller number of liquid stools from either the kaolin-pectin combination or pectin alone. However, because of the lack of sufficient information, it could not be adequately evaluated. The agency concludes that the available information is insufficient to include monograph directions for kaolin for children 3 to under 12 years of age. Adequate data from a double-blind, placebo-controlled study in pediatric subjects with acute nonspecific diarrhea is needed to support the safety and effectiveness of kaolin for use in this age group.

Based on the studies evaluated, the dosage for kaolin in this final monograph is: Adults and children 12 years of age and over: oral dosage is 26.2 g after each loose stool. Continue to take every 6 hours until stool is firm but not more than 2 days. Do not exceed 262 g in 24 hours. Children under 12 years of age: ask a doctor.

(Comment 12) One comment contended that the proposed labeling indications are too detailed and technical and, thus, will not be understood by persons of low comprehension. The comment argued that many users of OTC drug products have little education and take these products on their own without the direction of a physician, clinician, nurse, or pharmacist. To simplify the labeling for persons of low comprehension, the comment suggested that the statement of identity be "for diarrhea" instead of "antidiarrheal." The comment also suggested that the indication "Reduces the number of bowel movements in diarrhea" be changed to "Decreases bowel movements" or "Reduces bowel movements."

The agency agrees. Section 335.50(a) in this final rule gives manufacturers the option of using either "antidiarrheal" or "for diarrhea" as the statement of identity for these products. The agency modified the indication to "reduces number of bowel movements" and included it as an additional optional claim for products containing bismuth subsalicylate (see section III this document).

(Comment 13) One comment stated that there was a contradiction in the indications proposed in § 335.50(b) (51 FR 16138 at 16149). The comment noted that the agency stated that it was recommending that the indications "For the treatment of diarrhea" or "Controls (stops) diarrhea" be used in the labeling of OTC antidiarrheal drug products, but these indications were not included in the proposed monograph (51 FR 16138 at 16140 to 16141). The comment also suggested that "relieves pain in diarrhea" be a monograph indication. The comment stated that these indications are good, simple, and understandable and should be adopted by the agency.

The comment is correct that the indications "For the treatment of diarrhea" or "Controls (stops) diarrhea" were not included in the TFM. In comment 10 of the TFM (51 FR 16138 at 16140 to 16141), the agency stated that one or more of the following indications could be used depending upon the results of studies conducted on the ingredient contained in the

product: (1) "For the treatment of diarrhea" or "Controls (stops) diarrhea"; (2) "Reduces the number of bowel movements in diarrhea"; and (3) "Improves consistency of loose, watery bowel movements in diarrhea." Based on the data on attapulgit, calcium polycarbophil, and polycarbophil evaluated in the TFM, only the second and third indications were proposed at that time.

The agency would not object to use of the indication "relieves pain in diarrhea," provided studies support this claim. In the TFM (51 FR 16138 at 16141), the agency stated that there are other symptoms that are secondary to diarrhea, such as abdominal pain or cramps, and that some antidiarrheal ingredients may also act to relieve these symptoms. However, adequate supporting data have not been submitted to date.

(Comment 14) One comment requested revisions in the warning proposed in § 335.50(c), which stated: "Do not use for more than 2 days, or in the presence of fever, or in children under 3 years of age unless directed by a doctor." The comment recommended: "If diarrhea continues for more than 2 days or is accompanied by a fever, consult your doctor." The comment stated that the agency's proposed wording inappropriately suggests that consumers should be concerned about safety of the product if it is used for more than 2 days or in the presence of fever. The comment contended that its revision would alert consumers to the serious conditions that may be indicated by prolonged diarrhea or diarrhea accompanied by fever and would emphasize the need for medical attention because of the disease condition, not because of drug use, as might be inferred from the agency's proposed warning. The comment also recommended deletion of the part of the proposed warning regarding use in children under 3 years of age because it is redundant with information that appears in the directions section. The comment explained that the directions proposed in § 335.50(d) advise that these products should not be used in children under 3 years of age without consulting a doctor and the professional labeling proposed in § 335.80 provides health professionals information about using these products in children under 3 years of age.

The agency agrees that the information about use in children is repetitious and could be deleted. The directions in § 335.50(d) in this final monograph advise to "ask a doctor" for children under 12 years of age. The final monograph does not include proposed