

calcium hydroxide, charcoal (activated), potassium carbonate, or rhubarb fluidextract for antidiarrheal use.

The cost to reformulate a product will vary greatly depending on the nature of the change in formulation, the product, the process, and the size of the firm. Some of the manufacturers of the 50 products containing nonmonograph active ingredients may elect not to reformulate (*i.e.*, they may elect to discontinue marketing of the product). For those products that need reformulation, the cost can be significant. Because of the other monograph active ingredients available for reformulation, no manufacturer should need to change its dosage form; however, it will have to redo the validation (product, process, new supplier), conduct stability tests, and change master production records in order to ensure compliance with current good manufacturing practice. (See section 501(a)(1)(B) of the act (21 U.S.C. 351(a)(1)(B) and parts 210 and 211 (21 CFR parts 210 and 211).) The agency estimates the cost of reformulation to range from \$100,000 to \$500,000 per product. Therefore, if all 50 products are reformulated, the midpoint of the cost estimate implies total costs of \$15 million. However, the agency believes the total costs will be much smaller because not all manufacturers will elect to reformulate and some may choose to discontinue a product line if sales are too low to justify the added cost and/or they also produce substitute products that do not require reformulation. Manufacturers may also elect to purchase reformulated products from another manufacturer and then be a distributor of that product.

Because these products must be manufactured in compliance with the pharmaceutical current good manufacturing practices (parts 210 and 211), all firms would have the necessary skills and personnel to perform these tasks either in-house or by contractual arrangement. The final rule does not require any new reporting or recordkeeping activities. No additional professional skills are needed.

This final rule establishes the monograph for OTC antidiarrheal drug products and will require relabeling of all products covered by the monograph. Estimates of relabeling costs for the type of changes required by this rule vary greatly and range from \$500 to \$15,000 per stockkeeping unit (SKU) (individual products, packages, and sizes) depending on whether the products are nationally branded or private label. The agency assumes the same weighted average cost to relabel (*i.e.*, \$3,600 per SKU) that it estimated for the final rule

requiring uniform label formats of OTC drug products (64 FR 13254 at 13279 to 13281). Assuming 350 to 400 affected OTC SKUs in the marketplace, total one-time costs of relabeling would be \$1.26 to 1.44 million. Because frequent labeling redesigns are a recognized cost of doing business in the OTC drug industry, these costs may be less. Manufacturers that make voluntary market-driven changes to their labeling during the implementation period can implement the regulatory requirements for a nominal cost.

This final rule may have an economic impact on some small entities. The agency's drug listing system indicates that about 350 to 400 products will need to be relabeled, and that this relabeling will be prepared by about 45 manufacturers, most of which are private label or contract manufacturers. Based on the Small Business Administration's determination that a small firm in this industry has fewer than 750 employees, roughly 70 percent of the firms are considered small. The economic impact on any particular firm is very difficult to measure, because it will vary with the type and number of products affected, the number of SKUs per product, and the ability to coordinate these label changes with those required for other purposes. For example, assuming average industry costs, a small company that had 5 products with 3 SKUs each for a total of 15 SKUs would experience a one-time cost of \$54,000. A small private label manufacturer with the same product line and 10 customers per SKU, for a total of 150 SKUs, would experience a one-time cost of \$540,000. If one or more products needed to be reformulated, the costs would increase by \$100,000 to \$500,000 per formulation.

Some of these relabeling costs will be mitigated because the agency is allowing 12 months for manufacturers to implement the required labeling revisions for all products containing antidiarrheal active ingredients. Products with annual sales less than \$25,000 have 12 additional months. Therefore, many of the labeling revisions may be done in the normal course of business. Among the steps the agency is taking to minimize the impact on small entities are: (1) Providing enough time for implementation to enable entities to use up existing labeling stock, and (2) allowing the labeling changes required by this final monograph to be implemented concurrently with the labeling changes required by the new OTC drug labeling format final rule. The agency believes that these actions provide substantial

flexibility and reductions in cost for small entities.

The agency considered but rejected several labeling alternatives: (1) A shorter or longer implementation period, and (2) an exemption from coverage for small entities. While the agency believes that consumers would benefit from having this new labeling in place as soon as possible, the agency also acknowledges that coordination of the labeling changes resulting from implementation of the new OTC "drug facts" labeling and the antidiarrheal final rule may significantly reduce the costs of this final rule. A longer time period would unnecessarily delay the benefit of new labeling and revised formulations, where applicable, to consumers who self-medicate with these OTC antidiarrheal drug products. The agency rejected an exemption for small entities because the new labeling and revised formulations, where applicable, are also needed by consumers who purchase products marketed by those entities. However, a longer compliance date (24 months) is being provided for products with annual sales less than \$25,000.

This analysis shows that the agency has undertaken important steps to reduce the burden to small entities. This economic analysis, together with other relevant sections of this document, serves as the agency's final regulatory flexibility analysis, as required under the Regulatory Flexibility Act.

VI. Paperwork Reduction Act of 1995

FDA concludes that the labeling requirements in this document are 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 labeling statements are 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

The agency 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 final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not