

to be safe and effective for their labeled indications under ordinary conditions of use as those terms are defined in the act. This judgment balances the benefits of these drug products against their potential risks (see § 330.10(a)).

FDA's decision to act in this instance need not meet the standard of proof required to prevail in a private tort action (*Glastetter v. Novartis Pharmaceuticals, Corp.*, 252 F.3d 986, 991 (8th Cir. 2001)). To mandate warnings, or take similar regulatory action, FDA need not show, nor do we allege, actual causation. For an expanded discussion of case law supporting FDA's authority to require such warnings, see "Labeling of Diphenhydramine-Containing Drug Products for Over-the-Counter Human Use, Final Rule" (67 FR 72555, December 6, 2002).

VI. Analysis of Impacts

An analysis of the costs and benefits of this regulation, conducted under Executive Order 12291, was discussed in the TFM for OTC antiperspirant drug products (47 FR 36492 at 36503). The one comment received is addressed in section II.A, comment 4 of this final rule and further addressed later in this section.

FDA has examined the impacts of this final 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). Under the Regulatory Flexibility Act, if a rule has a significant economic impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the 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 in any one year by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million (adjusted annually for inflation). The proposed rule that has led to the development of this final rule was published on August 20, 1982, before the Unfunded Mandates Reform Act of 1995 was enacted. This final rule will not result in an expenditure in any one year by State,

local, and tribal governments, in the aggregate, or by the private sector, of \$100 million.

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

FDA has determined that this final rule will not have a significant economic impact on a substantial number of small entities. While the exact number of affected small entities is difficult to determine at any given time, the agency received only one comment from a small entity, which is discussed later in this section. This discussion explains the agency's determination that this final rule will not have a significant economic impact on a substantial number of small entities.

The purpose of this final rule is to establish conditions under which OTC antiperspirant drug products are generally recognized as safe and effective and not misbranded. This includes establishing the allowable monograph ingredients and labeling. Eighteen of the 19 active ingredients under review are included in the final monograph. The remaining ingredient could have been included had a USP–NF monograph been developed for this ingredient. If a USP–NF monograph is developed before the effective date of this final monograph, products containing this ingredient could continue to be marketed without reformulation. Without a USP–NF monograph for the ingredient, product reformulations to include a monograph antiperspirant active ingredient or discontinuation of the products will need to occur. The agency believes that this one antiperspirant active ingredient is currently in only a few products. Based on the large number of antiperspirant drug products in the OTC marketplace and the vast array of products that one known affected company currently markets, the agency considers the required reformulation or discontinuation of a few products not to be overly burdensome or substantial. The one known affected company markets at least 30 products not affected by this final rule. Only one of its products includes the active ingredient

excluded under the final rule. Any company using this active ingredient has the option to: (1) Reformulate using any of the 18 active ingredients included in this final rule, (2) reformulate without this active ingredient and market the product as a deodorant, or (3) discontinue the product.

This final rule establishes the monograph labeling for OTC antiperspirant drug products and will require relabeling of all products covered by the monograph. The agency's Drug Listing System identifies approximately 200 manufacturers and 700 marketers of 1,300 OTC antiperspirant drug products containing the 19 ingredients covered by this final rule. It is likely that there are additional products that are not currently included in the agency's system. While it is difficult to determine an exact number, the agency estimates that about 1,500 OTC antiperspirant drug products will need to be relabeled based on this final rule.

The agency has been informed that relabeling costs of the type required by a final monograph generally average about \$3,000 to \$5,000 per stock keeping unit (SKU) (individual products, packages, and sizes). However, some of the relabeling that occurs as a result of this specific final monograph will be due to additional indications that the agency has included in the final monograph and that manufacturers will wish to add to their labeling. Assuming that there are about 1,300 to 1,500 affected OTC SKUs in the marketplace, total one-time costs of relabeling would be \$3.9 million (\$3,000 per SKU x 1,300 SKUs) to \$7.5 million (\$5,000 per SKU x 1,500 SKUs). The agency believes that actual costs will be lower for several reasons. First, many of the label changes will be made by private label manufacturers that tend to use relatively simple and less expensive labeling. Second, the agency has finalized a revised labeling format for OTC drug products in § 201.66. The agency is allowing manufacturers to incorporate the labeling changes required by this final rule along with the new general OTC drug labeling format. Thus, the relabeling costs resulting from two different but related final rules will be individually reduced by implementing both required changes at the same time.

Some relabeling costs will be further reduced because the agency is allowing up to 18 months (24 months for products with annual sales less than \$25,000) for these revisions so they may be done in the normal course of business. Thus, manufacturers who