

at 6828). The Panel's reference to symptoms of dryness was not included in the TFM because the agency considers the use of skin protectants for dryness to be a cosmetic claim. The agency has now determined that it should not have included the "sunburn" claim in the TFM because the only context in which the Panel discussed it was cosmetic in nature.

The agency is also concerned that skin protectants may inappropriately be used for "sunburn" because the data indicate that it is not desirable to apply a skin protectant to sunburn that has just occurred. As the Panel noted, when petrolatum is applied to sunburn, evaporation is curtailed (43 FR 34628 at 34639). The agency is concerned that application of skin protectants, such as petrolatum and the other ingredients for which the Panel recommended a dryness claim for sunburn, to sunburn that has just occurred would occlude the area and prevent evaporation from occurring or significantly reduce evaporation. Thus, there are no data in the administrative record for this rulemaking to support a "protection of sunburn" claim for these ingredients. The agency would consider including such a claim for these ingredients, however, if adequate supporting data are provided.

The agency has determined that insufficient data were submitted to include the words "to allow healing to begin" and to include uses for heat rash, burning feet, and foot discomfort in § 347.50(b)(3). The agency concludes that the expanded "uses" section in this final monograph provides manufacturers an adequate number of options for labeling OTC skin protectant drug products.

(Comment 8) One comment mentioned that no wound healing claim or Category I labeling was provided for three skin protectant ingredients: Allantoin, live yeast cell derivative (LYCD), and zinc acetate.

The Panel classified these ingredients as Category III skin protectants for wound-healing based on the lack of effectiveness data (43 FR 34628 at 34644 through 34647). Insufficient data were submitted for LYCD (*see* section II, comment 25 of this document) and no additional data were submitted for allantoin or zinc acetate to support a "wound healing" use.

(Comment 9) One comment requested that compound benzoin tincture be included as a Category I topical skin protectant. The comment mentioned the conclusion of the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products (Cough-Cold Panel) that

compound benzoin tincture was safe for use in boiling water as a steam inhalant for expectorant purposes (41 FR 38312 at 38360, September 9, 1976). The comment also cited the recommendation of the Advisory Review Panel on OTC Dentifrice and Dental Care Drug Products (Dental Panel) that compound benzoin tincture was safe and effective for use as an oral mucosal protectant (47 FR 22712 at 22746 and 22747, May 25, 1982). The comment cited acceptance of compound benzoin tincture in several pharmacopeias, experience over decades of use, and the low incidence of adverse reactions or significant side effects in the published literature. The comment cited several skin protectant uses from well-established references or current product labeling: "* * * to small cuts and to intact skin under occlusive plasters and bandages" (Ref. 5), "* * * ulcers, bedsores, cracked nipples, and fissures of the lips and anus" (Ref. 6), and "apply to the skin under adhesive dressings, to treat skin fissures and bedsores, to reduce skin sensitivity to adhesive plasters, and to prevent skin irritation in ischemic areas" (Ref. 7).

Compound benzoin tincture is included in the *USP* as a fixed formulation containing 10 percent benzoin, 2 percent aloe, 8 percent storax, 4 percent tolu balsam, and 74 to 80 percent ethanol (Ref. 8). The agency finds that use as a steam inhalant for expectorant purposes evaluated by the Cough-Cold Panel (41 FR 38312 at 38360) has little relevance to use as a skin protectant. Although the agency acknowledges that standard references (Refs. 5 and 6) and literature articles describe numerous uses for compound benzoin tincture, no data from controlled clinical studies were provided.

Gosselin et al. (Ref. 9) indicated that the alcohol in benzoin tincture would be responsible for major toxic effects if ingested. The Dental Panel discussed literature reports of three cases of irritation and hypersensitivity resulting from topical use of benzoin tincture (47 FR 22712 at 22746 and 22747). In addition, the published literature contains numerous other reports of allergic contact dermatitis and sensitivity attributed to compound benzoin tincture and benzoin tincture. Cullen, Tonkin, and May (Ref. 10) stated that the literature was replete with reports of cutaneous sensitivity to compound benzoin tincture and its components, citing reports following local application. Rademaker and Kirby (Ref. 11) reported two cases of bullous contact dermatitis to a skin adhesive spray and mentioned that Fisher (Ref.

12) recommends that benzoin no longer be used as a skin adhesive. Marks and Rainey (Ref. 13) and James, White, and Yanklowitz (Ref. 14) reported other cases of allergic contact dermatitis. Sixteen cases resulted when benzoin was applied to prevent friction blisters. Other authors report contact dermatitis from benzoin used as an ingredient in greasepaint makeup (Ref. 15) and as an antioxidant in food additives (Ref. 16). In addition, benzoin provokes pemphigus erythematosus (Ref. 17), complicates management of venous leg ulcers (Ref. 18), and adversely affects wound healing after circumcision in children (Ref. 19).

Based on these reports of adverse events and the availability of other monograph skin protectant ingredients, the agency concludes that compound benzoin tincture is not safe for use as a general OTC skin protectant ingredient and would be inappropriate for many of the uses included in this final monograph.

(Comment 10) One comment requested that camphorated metacresol be included as an active ingredient in the final monograph for OTC skin protectant drug products, as long as the amount of metacresol did not exceed 1.5 percent (by weight) and the amount of camphor did not exceed 3 percent. Noting that phenol (0.5 to 1.5 percent) and camphor (0.1 to 3 percent) were proposed Category I ingredients in the TFM for OTC external analgesic drug products (48 FR 5852 at 5867, February 8, 1983) and citing an agency letter (Ref. 20) agreeing that metacresol was less toxic than phenol, the comment contended that there should be no safety concern about products containing camphor and metacresol in these concentrations.

Because information has not been provided to demonstrate a skin protectant effect, camphorated metacresol is not included in this final monograph.

(Comment 11) One manufacturer submitted data and information (Refs. 21 and 22) to FDA's Miscellaneous External Panel in response to the call-for-data notice published in the **Federal Register** of November 16, 1973 (38 FR 31697). The data were for a drug product containing water-soluble chlorophyllins in an ointment and a solution dosage form with a label indication "to promote healing and to relieve itching and discomfort of minor wounds, burns, surface ulcers, cuts, abrasions and skin irritations."

The Miscellaneous External Panel was disbanded before reviewing these submissions. Subsequently, because the product label contained a claim for