

wound healing and products with this claim had previously been included in the skin protectant rulemaking, the agency placed the submissions in the skin protectant rulemaking as a comment to the February 15, 1983, TFM, and the manufacturer submitted a more recent study on effectiveness for wound healing (Ref. 23).

The Dental Panel evaluated water-soluble chlorophyllins as oral wound healing agents in its report on OTC oral mucosal injury drug products (44 FR 63270, November 2, 1979) and concluded that water-soluble chlorophyllins were safe but that there were insufficient data available to permit final classification of effectiveness for OTC use as an oral wound healing agent (44 FR 63270 at 63286). The agency accepted the Dental Panel's classification in the TFM for OTC oral mucosal injury drug products (48 FR 33984 at 33991, July 26, 1983). No additional data were submitted and, in the final rule (51 FR 26112, July 18, 1986), the agency included water soluble chlorophyllins in the list of nonmonograph ingredients in 21 CFR 310.534.

The agency has reviewed the manufacturer's submissions (Refs. 21, 22, and 23). One submission (Ref. 21) contained information on various kinds of wounds that were treated with water-soluble chlorophyllins by health-care professionals. None were self-treatment conditions. Another (Ref. 22) contained translations of three foreign articles reporting laboratory and animal studies on water-soluble chlorophyllins that contain background information but do not support general recognition of safety and effectiveness in humans. A research report (Ref. 23) did not assess OTC uses, lacked subject and placebo controls, and questioned whether the observed effects were due to the products or the manner of caring for the wounds.

The agency concludes that the data submitted do not support effectiveness of water-soluble chlorophyllins for promoting wound healing for conditions treated with OTC skin protectant drug products.

(Comment 12) Cod liver oil was not categorized by the Panel for use as an OTC skin protectant because it was not included among the labeled ingredients in marketed products submitted to the Panel for review. In evaluating cod liver oil for use in diaper rash drug products, the agency considered the long history of clinical use as a skin protectant ingredient (55 FR 25204 at 25213, June 20, 1990).

In the rulemaking for OTC anorectal drug products, the Advisory Review Panel on OTC Hemorrhoidal Drug

Products (Hemorrhoidal Panel) classified cod liver oil as Category I for use as an anorectal protectant and recommended a maximum daily dose of 10,000 I.U. (International Units equivalent to USP Units) for vitamin A and 400 I.U. for vitamin D (cholecalciferol) per 24 hours (45 FR 35576 at 35630, May 27, 1980). The Hemorrhoidal Panel stated that an extensive review of the literature on cod liver oil revealed no adverse effects when applied topically as a protectant and concluded that the effectiveness of cod liver oil, as a protectant, is due to its bland and soothing effect associated with its oily nature. In the TFM (53 FR 30756 at 30767, August 15, 1988) and final monograph (55 FR 31776 at 31780, August 3, 1990) for OTC anorectal drug products, the agency affirmed the Hemorrhoidal Panel's Category I classification and specified that cod liver oil may be used only in combination with one to three other protectant active ingredients.

The agency has surveyed the marketplace and determined that cod liver oil is marketed only in combination with other ingredients in several products with skin protectant claims (Refs. 3 and 24). One product contains 12.5 percent (Ref. 24), but in most cases the cod liver oil concentration is not provided.

Therefore, the agency is including cod liver oil as an active ingredient in skin protectant drug products in accord with § 347.20(a)(1) and (a)(2), only in combination with certain other skin protectant active ingredients, within the concentrations (5 to 13.56 percent) specified in § 347.10(e), provided that the product is labeled so that the amount of the product that is used in a 24-hour period represents a quantity that does not exceed 400 USP Units of vitamin D and 10,000 USP Units of vitamin A.

(Comment 13) In the notice of proposed rulemaking (54 FR 40808 at 40810), the agency stated that it was necessary to have publicly available chemical information for colloidal oatmeal. One manufacturer submitted a proposed standard for colloidal oatmeal, which it stated was patterned after standards for starch and psyllium (Ref. 25). The agency sent this information to the U.S. Pharmacopeial Convention (USPC) (Ref. 26). Compendial standards were proposed in the Pharmacopeial Forum of January and February 1992 (Ref. 27) and a final *USP* monograph became effective on November 15, 1992 (Ref. 28).

(Comment 14) One comment requested that colloidal oatmeal be included in the skin protectant

monograph as a safe and effective ingredient for the claim: "For prompt temporary relief of itchy, sore, sensitive skin due to rashes, eczema/psoriasis, hemorrhoidal and genital irritations, diaper rash, chicken pox, prickly heat, hives, poison ivy/oak, and sunburn." The comment cited references (Refs. 29 through 33) to support this claim.

The agency previously discussed poison ivy/oak claims in comment 1 of the skin protectant poison ivy, oak, and sumac notice of proposed rulemaking (54 FR 40808 at 40809 to 40811). The agency has determined the additional references cited by the comment show that colloidal oatmeal can provide temporary skin protection and relieve minor irritation and itching due to a number of conditions. Further, the agency has no adverse reaction reports on file for colloidal oatmeal. Thus, the agency is expanding the indications for colloidal oatmeal in § 347.50(b)(4) in this final monograph. In addition, manufacturers can opt to select one or more of the "due to" conditions to list in the product's labeling. However, since no data were submitted using colloidal oatmeal for chicken pox, sunburn, or hives, these indications are nonmonograph. The agency will discuss a "prickly heat" claim in the skin protectant diaper rash drug products final rule.

(Comment 15) Two comments noted that the agency's proposed directions in § 347.50 (54 FR 40808 at 40818) for the use of colloidal oatmeal as a soak in a tub do not allow for the range of use concentrations or dosage forms that have been reported in the clinical literature and requested that FDA specify a use concentration range. The comment stated that colloidal oatmeal is unusual in comparison to other barrier skin protectants because it is often intended for dispersion in water and is formulated in a variety of other dosage forms.

One comment summarized and calculated the colloidal oatmeal concentrations used in baths (Refs. 32 and 34 through 41). The comment noted that the most common concentration ranges of colloidal oatmeal are from 0.007 to 10 percent in use but added that colloidal oatmeal is present in commercial products from 1 to 100 percent. Another comment recommended changing the proposed directions in § 347.50(d)(2) from one "cupful" to "up to a cupful."

The agency has reviewed the recommended concentrations of colloidal oatmeal reported in the literature and reference texts (Refs. 4, 29 through 32, 34 through 45, 47, 48, and 49) and has considered the range of