

administrative record for this TFM closed on April 9, 1984. The administrative record for this rulemaking was last reopened on November 19, 1997 (62 FR 61710) to include safety and effectiveness data on OTC vaginal douche drug product ingredients for external analgesic uses (e.g., povidone-iodine for the relief of minor vaginal itching and irritation) and closed on February 17, 1998. Under § 330.10(a)(7)(v), new data and information submitted after February 17, 1998, prior to the establishment of a final monograph (FM), are considered a petition to amend the monograph and are to be considered only after a FM has been published unless the agency finds that good cause has been shown that warrants earlier consideration. Further, under § 330.10(a)(10)(ii), FDA shall make all decisions and issue all orders under § 330.10 in the FM solely on the basis of the administrative record and shall not consider data or information not included as part of the administrative record.

FDA has received new data and information submitted to the external analgesic rulemaking after the administrative record closed on April 19, 1984. In some cases, interested persons submitted a petition to reopen the record. In other cases, they submitted new data and information to the Division of Dockets Management as comments on the TFM. A number of the petitions and comments submitted to the TFM contain new data on proposed nonmonograph (Category II and Category III) ingredients and on external analgesic active ingredients applied in a patch, plaster, or poultice dosage form.

II. Reopening of the Administrative Record

Because these data are relevant to the final classification of these ingredients in the FM, FDA has determined that good cause exists to consider these new data and information in developing the FM for these products. By this document, FDA announces that it is treating all of these submissions, received after the administrative record closed, as petitions to reopen the administrative record, and is granting the petitions by allowing the new data and information contained therein to be included in the administrative record for the rulemaking for OTC external analgesic drug products. Accordingly, the agency is reopening the administrative record for this rulemaking to accept data and information previously submitted to the Division of Dockets Management into the administrative record and to provide interested persons an opportunity to

submit comments on these data and information prior to the closing of the record.

III. Status of Patch, Plaster, and Poultice Dosage Forms for OTC External Analgesic Drug Products

After the TFM was published on February 8, 1983, FDA received a petition (Ref. 1) to amend portions of the TFM to add poultice or plaster dosage forms only for the counterirritant ingredients in proposed § 348.12, specifically for the ingredients methyl salicylate; camphor; menthol; and capsicum. This petition led FDA to review the report of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (the Panel) (44 FR 69768, December 4, 1979), the TFM for OTC external analgesic drug products, available data, marketing history, and the current market for OTC counterirritant ingredients in topical drug products used in poultice and plaster dosage forms.

FDA found that the Panel discussed poultices and plasters only in its discussion of allyl isothiocyanate (oil of mustard) (44 FR 69768 at 69791 and 69792) and stated its concern that used as a poultice, the inflammatory action caused by allyl isothiocyanate may go beyond erythema to vesication. It was the Panel's opinion that although the actual number of adverse effects to external use of mustard preparations was relatively low, care should be taken to assure that safety is maintained through adequate packaging, labeling, and application. The low incidence of adverse reactions the Panel discussed (44 FR 69768 at 69791) was for an ointment dosage form (Ref. 2) and not for a plaster or poultice (a soft, moist mass about the consistency of cooked cereal, spread between layers of muslin, gauze, or towels and applied hot to a given area in order to create moist local heat or counterirritation). The Panel did briefly discuss mustard plaster, National Formulary IX, but did not include a plaster dosage form in its recommended dosage for this ingredient (44 FR 69768 at 69792).

The Panel did not discuss plaster or poultice dosage forms for any other counterirritants, although articles from standard texts in some of the submissions to the Panel indicated that capsicum has been used in a plaster dosage form (Ref. 3). There was one submission to the Panel for a medicated poultice dressing containing methyl salicylate, salicylic acid, and eucalyptus oil as active ingredients (Ref. 4). Although the Panel recommended a

Category I classification for methyl salicylate, it did not discuss the submission related to the use of this ingredient as a poultice or plaster. The submission did not contain any controlled clinical evaluations to support safety and effectiveness of the combination drug product or for the specific contribution of the individual active ingredients. The product's safety and effectiveness were based on its performance for 80 years. At that time, FDA surveyed several standard texts that listed currently marketed topical drug products containing counterirritants and did not find any plaster or poultice dosage forms listed therein.

FDA stated (Ref. 5) that in order for poultice and plaster dosage forms to be generally recognized as safe and effective and to develop any additional labeling that may be needed for such dosage forms, it is necessary to obtain more information, specifically:

1. The safe and effective concentration of the drug ingredient(s), especially under the occlusion of a plaster.
2. Data on percutaneous absorption under occlusion.
3. The length of contact time that it is safe to leave the poultice or plaster on the skin; how often the plaster or poultice needs to be changed for effective use.
4. The frequency of application that is considered safe and effective.
5. Whether or not directions and a warning are necessary regarding checking the area at specified intervals for erythema to prevent blistering, and what time intervals are recommended.
6. The age groups for whom poultices and plasters are recommended for safe use.
7. Labeling of currently marketed products.

FDA's detailed comments are on file in the Division of Dockets Management (Ref. 5).

Since that time, FDA has received a number of submissions on external analgesic counterirritant active ingredients in a plaster dosage form (Refs. 6 through 31). The submissions have included protocols and data to establish safety and effectiveness of the plaster/patch dosage forms. FDA has commented on the protocols and data, but has not found the information sufficient to support the safety and effectiveness of these dosage forms (Refs. 32 through 44). Further, FDA is not aware of sufficient data to classify any OTC external analgesic active ingredient in a patch, plaster, or poultice dosage form as Category I. Accordingly, FDA is classifying all OTC