



2 REGULATORY HISTORY

On November 16, 1988, the Agency issued the Tentative Final Monograph (TFM) for Internal Analgesic Drug Products which established conditions under which OTC IAAA drug products are generally recognized as safe and effective [53 FR 46204]. Ibuprofen was not included in the TFM. Ibuprofen has been approved for OTC use in adults and children 12 years and older since 1984. Approval was obtained through the new drug application (NDA) process. A single OTC ibuprofen dose is 200 to 400 mg up to a maximum of 1,200 mg daily.

On November 25, 1997, the Agency received a citizen's petition to amend the OTC IAAA TFM to include the oral dosage form of ibuprofen 200 mg. The petition asserted that ibuprofen had been used for a material extent and for a material time as an internal analgesic and antipyretic under nonprescription conditions. The petition also provided a summary of safety and effectiveness data for OTC dosages of ibuprofen.

In response to this citizen's petition, FDA published a Proposed Rule in the August 21, 2002 *Federal Register* [67 FR 54139] to amend the TFM for OTC IAAA drug products to include ibuprofen 200 mg tablets as a generally recognized safe and effective analgesic/antipyretic active ingredient for adult OTC use. In addition, FDA also proposed amending its regulations to include consistent allergy warnings for all OTC IAAA drug products containing nonsteroidal anti-inflammatory active ingredients (NSAIDs).

On September 20, 2002, FDA held a meeting of the Nonprescription Drugs Advisory Committee (NDAC) to discuss safety issues related to the use of aspirin and other OTC nonsteroidal anti-inflammatory drugs (NSAIDs), including ibuprofen. FDA asked the NDAC to consider if additional warnings or other risk management strategies were needed to alert the consumer with regard to potential gastrointestinal bleeding and renal insufficiency related to the OTC use of these drug products. At this meeting, the NDAC members also discussed other OTC NSAID labeling topics that were not included in FDA's Proposed Rule of August 21, 2002. However, FDA indicated that discussions at the meeting might be considered as comments to the Proposed Rule.

On June 4, 2003, the comment period on the Proposed Rule of August 21, 2002 was reopened via a *Federal Register* announcement [68 FR 33429] to provide additional time to fully evaluate the impact of NDAC discussions of OTC IAAA drug products, including

ibuprofen, at its September 20, 2002 meeting and to evaluate the proposed additions of August 21, 2002 to the TFM.