



February 17, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland, 20852

RE: Docket 2000N-1449 - Agency Information Collection Activities; Comment Request; Guidance for Industry – Changes to an Approved New Drug Application or Abbreviated New Drug Application.

Merck & Co., Inc is a leading worldwide, human health products company. Through a combination of the best science and state-of-the-art medicine, Merck's Research and Development (R&D) pipeline has produced many important pharmaceutical products available today. These products have saved the lives of or improved the quality of life for millions of people globally.

Federal register Notice [Docket No. 2000N-1449] solicits comments on the collection of information contained in guidance for industry entitled "Changes to an Approved NDA or ANDA." In response to this notice, the following information is provided to supplement the accuracy of FDA's estimate of the burden of the proposed collection of information. We are well-qualified to provide an estimate of regulatory burden due to our vast experience with the preparation of various categories of NDA supplements.

Under section 506 A(d)(3)(A) of the Federal Food, Drug, and Cosmetic Act: information developed by the applicant to validate the effects of manufacturing changes on the identity, strength, quality, purity, and potency is required to be submitted to FDA as part of a supplement or annual report. Preliminary assessment within Merck of average estimates of time required to support process validation for solid oral dosage formulations is approximately 3 months and approximately 6 months for sterile formulations. Given this assessment, our assumption made in review of the data presented as "Hours per Response" in Table 1 of the Notice, is that the values (ranging from 35 to 150 hours, depending on category) represent average time spent by Industry in the preparation and submission of supplements and annual reports. It does not appear to incorporate reliable estimates of the time required to support validation of the effects of the change under Section 506 A of the act.

Based on this assumption, an evaluation was performed within Merck to assess the average time spent by scientists to prepare CMC regulatory documentation according to the required reporting category. The evaluation incorporated assembling documentation required to support various levels and types of post approval changes for drugs, other than specified biotechnology and specified synthetic biological products, as cited within the Guidance for Industry – Changes to an Approved NDA or ANDA. In addition to the level of regulatory reporting category, the results of our evaluation supported the relative association between levels of regulatory burden and the type/number of post approval changes proposed. It should be noted that the resulting regulatory burden may also be dependent on product specific requirements relating to formulation or production.

Our results approximated an average of 185 hours for preparation of prior approval supplements and ranged from approximately 100 to 250 hours depending on type/number of changes proposed. An average of approximately 160 hours was estimated for preparation of CBE/CBE-30 supplements with a range from 130 to 215 hours depending on type/number of changes proposed. An average of approximately 130 hours was estimated for preparation of annual reports.

As noted herein, we are providing our estimates of the amount of time required not only to prepare the supplement, but to appropriately validate the manufacturing change. By our estimates, the Agency has somewhat underestimated the amount of time required to prepare the supplement and has not adequately considered the amount of time required to validate the change. We recommend that FDA reassess its estimates of the regulatory burden of preparing the various types of post-approval changes to include in its assessment revised estimates of the amount of time that it takes to validate appropriately the manufacturing change.

We appreciate the opportunity to share our comments with respect to FDA's Agency Information Collection Activities; Comment Request; Guidance for Industry--Changes to an Approved New Drug Application or Abbreviated New Drug Application. Please do not hesitate to contact me, should you have any questions.

Sincerely,



for
Donald M. Black, MD, MBA
Vice President
Global Strategic Regulatory Development