

Bayer HealthCare
Consumer Care Division

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September 15, 2005

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

Leonard Baum, RPh
Vice President
Regulatory Affairs

Re: Docket 2005P-0048

**Response to Additional Comments on Citizen Petition for Aspirin
Professional Labeling Proposed Changes**

Dear Dr. Ellenberg:

Reference is made to McNeil Consumer & Specialty Pharmaceuticals' Citizen Petition (CP1) requesting FDA approval for a change in the professional labeling for aspirin dosing for secondary prevention of cardiovascular and cerebrovascular events submitted January 31, 2005. Reference is also made to Bayer Consumer Care's (Bayer) comments to this Petition submitted to the Agency on May 4, 2005 and McNeil's response on August 3, 2005 to Bayer's comments.

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Bayer has carefully assessed the available evidence and the response by McNeil and we fully stand by our position outlined in our May 4, 2005 submission regarding the currently approved dose range in the professional label of 75 – 325 mg aspirin for the secondary prevention of cardio- and 50 – 325 mg for cerebrovascular events. McNeil fails to present data which would address the key underlying issue that there is no compelling, long term prospective, comparative study proving equal efficacy or non-equal safety between the doses of aspirin in the range in question (50–325 mg) for the secondary prevention of both myocardial infarction and stroke.

The key data supporting the McNeil position (Serebruany, 2005) is from a meta analysis of existing data which is fraught with scientific and methodological shortcomings. The trials reviewed in this analysis cover a range of doses, many of which are not within the low dose range (50-325 mg) and therefore can skew the findings in both directions. Specifically, Serebruany, et al presented data from 31 clinical trials and divided the doses into three arbitrary groups of dose; <100 mg, 100 to 200 mg and >200 mg aspirin/day.

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The key issues remain:

1. Doses above 200 mg cannot be grouped together, when in fact several studies in Serebruanuy's analysis used doses above 1000 mg.
2. Doses above 200 mg cannot be equated to a 325 mg daily dose. Data above this skews the safety findings presented compared to the efficacy of the 50-325 mg dose.

Thus, the authors do not make the comparison of doses of interest (50 - 325 mg / day).

These and other critical scientific comments have been submitted in direct response to the Serebruanuy meta analysis and accepted for publication (American Journal of Cardiology, In Press). As noted in our May 4, 2005 submission, when the analysis is limited to trials using doses in the low dose range (75 – 325 mg / day) there is no difference in hemorrhagic events.

We continue to acknowledge that there is no definitive evidence addressing comparative differences in the efficacy for doses between 75 and 325 mg. However, physicians are actively utilizing the entire range of aspirin doses (including 325 mg). This practice of recommending various doses for various CV conditions is based on the broad nature of the existing clinical trial evidence as well as physicians individual practice settings and patient populations.

Further, Bayer acknowledges that emerging data related to the area of aspirin resistance is not conclusive. Despite the preliminary nature of this information, there is an evolving body of evidence which should be considered (please refer to References 11 and 20-26 in our May 4, 2005 submission to the petition).

Again, Bayer believes that without persuasive, randomized clinical trial evidence that compares aspirin doses within the low dose range (50-325 mg.) and with emerging evidence considering the use of higher doses, a change to well-established indications is scientifically and clinically inappropriate.

Finally, McNeil notes in their August 3, 2005 comments that "Bayer's comments divert attention away from the important public health need..." Bayer takes great exception to McNeil's comments that Bayer is diverting attention away from public health need. In fact, Bayer strongly supports many national and international programs on the study of established and evolving clinical science of aspirin uses, particularly with regards to the risk reduction of cardiovascular disease and stroke.

In summary, Bayer stands by its original comments and supports the range of low dose aspirin (50 – 325 mg) currently approved in the professional aspirin labeling for secondary prevention of cardiovascular and cerebrovascular events. This range allows physicians to dose patients based on individual needs.

Thank you for your consideration of our comments as part of your review of this Citizen Petition. Should you have any questions, please feel free to contact me at 973-254-4672 or Catherine Fish, Senior Associate Director, Regulatory Affairs, at 973-254-4793.

Bayer HealthCare
Consumer Care Division

A handwritten signature in black ink, appearing to read 'L. Baum', written over a white background.

Leonard Baum, RPh
Vice President, Regulatory Affairs

Submitted in duplicate