Bayer HealthCare
Consumer Care Division

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Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
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Rockville, Maryland 20857

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RE: Docket 77N-0094

Request for February 2004 Public Feedback Meeting:
Follow Up to 12/8/03 Advisory Committee Hearing for
Aspirin Primary Prevention Labeling

Dear Dr. Ellenberg:

Bayer requests a meeting with representatives of the Cardio-Renal and OTC Divisions of FDA, as well as other Agency officials FDA may wish to have present, as a follow up to the December 8, 2003 Advisory Committee. The Committee was convened in December in response to a Citizen Petition (CP16) filed by Bayer in February 2003 for the consideration of primary prevention labeling for aspirin.

The Committee comments and FDA review provided valuable feedback that serve as the basis for the important discussion that would take place at such a meeting. There was apparent consensus within the Committee that an appropriate population exists for aspirin use in primary prevention. While Committee members voted negatively on certain FDA questions, many acknowledged both personal use and professional recommendation for aspirin in patient practice for primary prevention. The proceedings highlight the importance of our working together to meet the significant public health objective of reducing the burden of MI.

Bayer remains committed to working closely with the FDA and the medical community to address the remaining questions to ensure that the broadest appropriate use of aspirin is achieved.

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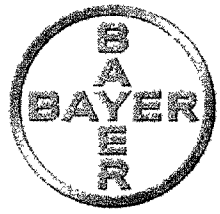
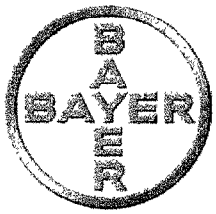
Questions for FDA Comment and Discussion

1. Many patients are at significant risk of MI in spite of not having a previous event. *Does the Agency agree that such patients could be at as high a risk as those currently approved for secondary prevention?*

2. Data from five Primary Prevention trials involving over 55,000 patients were presented in support of the proposed labeling for the use of aspirin in patients at moderate risk of MI. One of these studies in particular, TPT, included patients in the population of interest. While the other four studies were obviously of lower risk, they support the effectiveness of aspirin in "at risk" patients. *How can this robust database be used to support efficacy in moderate risk patients?*
   - As a point of reference, the approved use of aspirin for prevention in stable angina patients is based on a single study (SAPAT).
   - While the benefits observed in these studies are restricted to non-fatal MI, this represents an important and meaningful finding. *Does the FDA agree that a product that significantly reduces the most common form of MI should be so labeled?*
   - Because of difficulties in classifying silent MI, these events are usually excluded from study designs. *We are curious as to why the Agency placed so much emphasis on this endpoint (including the re-evaluation of studies to include the endpoint when not prospectively defined)?*
3. *Does FDA consider the number of female subjects studied sufficient to include women in the labeling, given that there were significantly more women in these 5 trials combined than the number of female subjects the Agency currently reviews as part of NDA approvals? If not, is FDA aware of any evidence to suggest women would differ from men with respect to aspirin's effects?*
   - There was a 10-year gap between the approval of aspirin use for recurrent stroke in men and women. The ten years between the 1988 Tentative Final Rule which excluded women and the 1998 Final Rule ultimately recognized that there were no gender differences in aspirin's benefit.



4. Major professional medical organizations including the American Heart Association, the American Diabetes Association and the United States Preventive Services Task Force support the Petition and have published guidelines for practicing physicians and recommend aspirin for primary prevention in those patients at sufficient risk suggesting that physicians can adequately assess risk. These organizations recognize the benefits/risks based on thorough review of the data and have determined the significant public health impact of broader appropriate use of aspirin. *Does FDA agree with the position of these bodies and if so, is FDA prepared to consider labeling similar to those suggested by these guidelines?*
5. The Agency is clearly comfortable with risk based labeling as evidenced by current statin labeling. *Is it the Agency's view that similar language could be constructed for aspirin? If not, does FDA have other approaches they would like considered and addressed?*
6. FDA prepared a medical report as briefing material to the Advisory Committee. The Agency stated that it was not in possession of all the original protocols associated with the key trials described in the Citizen Petition. *If the protocols for these studies could be obtained by the FDA, what questions might have been answered? Would the FDA like Bayer's assistance in helping to obtain the protocols?*
7. Based on the substantial evidence in favor of broader use of aspirin (and actual use in clinical practice), additional studies in this area appear unwarranted and unethical. *Does the FDA agree?*
    - It appears that FDA acknowledges the importance of aspirin being administered to patients in ongoing primary prevention studies for other drugs.
8. There have been over 200 studies involving more than 150,000 patients that have looked at the long term safety of aspirin. Bayer continues to believe that this large secondary prevention database, as well as, the 55,000 patients in the 5 primary prevention trials provides meaningful insight regarding the intended use. *Does the FDA agree that safety data from these studies is relevant to establishing the benefit to risk relationship for aspirin in moderate risk patients?*
9. Evidence was presented at the Advisory meeting highlighting the significant underutilization of aspirin in "at risk" patients (including those in currently approved indications). *How can Bayer in partnership with the FDA and the medical community develop labeling to help address this unfortunate public health reality?*



10. *Can the FDA provide an update on the timing and process for completing the review of the Petition?*
    - *How can Bayer work with the Agency to help address the apparent discrepancies between the investigator analyses and the Agency Medical Review?*

Bayer appreciates the opportunity to address this very important matter which will have significant impact on the public health in the United States.

Please contact me at 973-408-8181 at your earliest convenience to schedule this Feedback Meeting.

Bayer HealthCare
Consumer Care Division

Judy Doyle

Judy Doyle
Associate Director Regulatory Affairs

Desk Copies:

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