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Congress of the United States
House of Representatives
Washington, DC 20515-2107

July 12, 2006

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Andrew C. von Eschenbach, M.D.
Acting Commissioner
US Food and Drug Administration
U.S. Department of Health and Human Services
Parklawn Building
5600 Fishers Lane, Room 15-47
Rockville, MD 20857

Dear Dr. von Eschenbach:

I am writing in regard to a report on FDA's monitoring of postmarketing study commitments released by the Department of Health and Human Services Office of the Inspector General on July 7, 2006.

As you know, I have long been concerned about the FDA's monitoring of postmarketing studies and the FDA's ability to ensure that companies follow up on their postmarketing study commitments. Last year, I released a staff report, "Conspiracy of Silence: How the FDA Allows Drug Companies to Abuse the Accelerated Approval Process," which indicated that companies often do not complete postmarketing studies required as a condition of approval on a timely basis and the FDA does not enforce the requirement to complete these studies on a timely basis using the current regulatory mechanism and may need additional enforcement mechanisms to ensure timely completion of these studies.

I am very concerned about the new findings on this subject made in the Inspector General's (IG) report. According to the report, the IG found that:

1. FDA cannot readily identify whether or how timely postmarketing study commitments are progressing toward completion.
2. About one-third of annual status reports (ASRs) were missing or incomplete;
3. Even complete ASRs lack information that would be useful in monitoring the progress of postmarketing study commitments;
4. FDA has limited recourse when drug applicants do not submit required information or do not demonstrate progress in completing their postmarketing study commitments;
5. FDA lacks an effective management information system for monitoring postmarketing study commitments; and
6. Monitoring postmarketing study commitments is not a top priority at FDA.

Postmarketing studies are very important because often it is difficult to fully assess the safety or efficacy of a drug prior to approval. Therefore, in order to learn more about the risks and benefits of an approved drug, the FDA may ask companies to conduct postmarketing

studies, which are studies conducted after approval, while drugs are already on the market. Sometimes, such as in the case of accelerated approval, postmarketing studies are required as a condition of approval.

The Inspector General's findings are especially disturbing since the Government Accountability Office (GAO) reported similar findings in March 2006. The GAO reported that, the,

FDA lacks clear and effective processes for making decisions about, and providing management oversight of, postmarket safety issues. The process has been limited by a lack of clarity about how decisions are made and about organizational roles, insufficient oversight by management, and data constraints. GAO observed that there is a lack of criteria for determining what safety actions to take and when to take them. Certain parts of ODS's role in the process are unclear, including ODS's participation in FDA's scientific advisory committee meetings organized by OND. Insufficient communication between ODS and OND has been an ongoing concern and has hindered the decision-making process. ODS does not track information about ongoing postmarket safety issues, including the recommendations that ODS staff make for safety actions. FDA faces data constraints in making postmarket safety decisions. There are weaknesses in the different types of data available to FDA, and FDA lacks authority to require certain studies and has resource limitations for obtaining data.

In light of both the IG's findings and the GAO's, it is clear that the FDA needs to place a greater priority on postmarketing studies and reform the way that they track these studies and ensure their completion. In order to understand what actions, if any, the FDA is taking to address the issues raised in these two reports, I respectfully request responses to the following questions:

1. The Inspector General recommended that the FDA should instruct drug applicants to provide additional, meaningful information in their annual status reports on their open postmarketing study commitments. In particular the report recommends that the FDA require applicants to provide in their ASRs relevant dates of key milestones, including (1) submissions of study protocols, (2) completion of participant enrollment, (3) completion of studies, and (4) submissions of final reports. Will the FDA make changes to their annual status report requirement so that drug applicants are required to report additional information in the ASR? If so, please explain what changes will be made, what process will be taken to make those changes and the timeline for implementation? If not, why not? If changes in regulation are required to make changes to the ASR, will the FDA initiate a change in the regulations? If not, why not?
2. The IG recommended that the FDA improve the management information system for monitoring postmarketing study commitments so that it provides timely, accurate, and useful information. In particular, the IG recommended that the FDA:
 - a. Ensure that commitments are numbered uniquely and logically.

- b. Ensure that the database is populated with such useful information as the following items: (1) study start dates, (2) original scheduled completion dates, and (3) final report submission dates.
- c. Enhance the current reporting capability that identifies late ASRs and outstanding commitments.

Will the database system that the FDA is currently developing incorporate all of these recommendations? If not, which ones will it not include and why not? Will the database that incorporates these recommendations be publicly available? What is the timeline for implementation of this new database?

3. The IG recommended that “the FDA ensure that postmarketing study commitments are being monitored and that ASRs are being validated... To this end, FDA must ensure that reviewers have the information, tools, and time they need to complete this important task.” How many FTEs are currently working on ensuring that postmarketing study commitments are being monitored and that ASRs are being validated? How much of the FDA’s Fiscal Year 2006 budget is currently dedicated to monitoring postmarketing studies and validating ASRs? (Please provide dollar amount and percent of total budget.) How much of the FDA’s annual budget over the past 5 years has been spent on monitoring postmarketing studies and validating ASRs? (Please provide dollar amount and percent of total budget.) How much has been spent on creating and implementing the new postmarketing studies database up to July 1, 2006? How much does FDA anticipate spending on the project of reforming the postmarketing studies database?
4. Does FDA need more resources in order to better monitor postmarketing study commitments and review and validate annual status reports? If so, what resources does FDA need? If not, why not?
5. The IG also recommended that the “FDA should also consider seeking authority to obtain additional recourse options in cases of postmarketing study commitments that lag far behind schedule or for which required documents are not submitted. Currently, short of withdrawing a drug from the market—a remedy available to FDA only in limited circumstances—the only short-term, practical options available to FDA in dealing with drug applicants that do not comply with the terms of their commitments are sending letters and placing phone calls. Providing FDA reviewers with additional tools, such as the ability to impose monetary fines, may send a signal to drug applicants that there are consequences when postmarketing study commitments are not fulfilled.” Does the FDA agree with the IG’s assessment that “currently, short of withdrawing a drug from the market—a remedy available to FDA only in limited circumstances—the only short-term, practical options available to FDA in dealing with drug applicants that do not comply with the terms of their commitments are sending letters and placing phone calls”? If not, what other methods does the FDA use to ensure that companies comply with their requirements?

The Honorable Andrew von Eschenbach

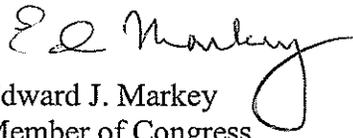
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6. Does the FDA agree with the IG's recommendation that the "FDA should also consider seeking authority to obtain additional recourse options in cases of postmarketing study commitments that lag far behind schedule or for which required documents are not submitted... Providing FDA reviewers with additional tools, such as the ability to impose monetary fines, may send a signal to drug applicants that there are consequences when postmarketing study commitments are not fulfilled." If so, what additional recourse options does the FDA believe would be useful and what steps is the FDA taking to seek additional authority? If not, why not?
7. According to the IG's report, the FDA disagreed with "[the IG's] finding that [the FDA] cannot readily identify whether and how timely postmarketing study commitments are progressing toward completion." If the FDA can readily identify whether and how timely postmarketing study commitments are progressing towards completion, I would appreciate it if the FDA could please provide me with a list of all of the current outstanding postmarket study commitments within 2 weeks. (Please provide all of the relevant information including Applicant name, Product name, Application number, Date of U.S. approval, Date of postmarketing study commitment, Description of postmarketing study commitment, Schedule for completion of and reporting on the postmarketing commitment, Status of the commitment, and Explanation of the status of the study.) If the FDA is not able to provide this information within two weeks, please explain why.

Thank you for your attention to this important issue. I respectfully request a response by July 26, 2006. If you have any questions regarding this request, please do not hesitate to contact Ms. Katharine Reinhalter at 202-225-2836. I look forward to your prompt reply.

Sincerely,



Edward J. Markey
Member of Congress