



August 5, 2005

Division of Dockets Management
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2005D-0062: Comments on FDA's Draft Guidance – "Drug Watch" for Emerging Drug Safety Information

Dear Sir or Madam:

Hoffmann-La Roche is pleased to provide input on the draft guidance entitled, "FDA's "Drug Watch" for Emerging Drug Safety Information". Our response is in the form of a general statement concerning the intent of the guidance and the overall issues to be addressed before the guidance is finalized. Outlined below are suggestions for modifications or alternatives for the Agency to explore.

General Comments:

We believe that all parties (regulators, sponsors, medical professionals and patients) agree with the Agency's purpose for the Drug Watch website -- to provide full disclosure and appropriate use of the latest information regarding the safety of a drug. However, building a website will not address this need and has the potential to mislead physicians and patients by providing preliminary, untested information.

Posting of emerging safety information based on a decision of the Drug Safety Oversight Board without the benefit of input from independent experts or the considerable expertise of the Sponsor is not a reasoned approach. It compromises the principle of providing balanced safety information because it eliminates the contribution from scientific discourse on the issue prior to public dissemination. We believe it is extremely unlikely that physicians and patients will be able to make better informed decisions by having access to unadjudicated, preliminary information. In fact, this approach will only add to the potential for misuse or misinterpretation of preliminary information, particularly by the lay press and consumers, which to some extent already exists. Posting of unadjudicated, preliminary information on an FDA site, even with extensive caveats, will provide credibility to potentially unfounded safety concerns before there is a systematic scientific evaluation. Even with caveats and disclaimers, it is unlikely that items posted on an FDA website would be considered by the public and the lay press as anything other than an official FDA position.

In addition, we believe FDA currently has in place the necessary procedures to obtain, evaluate and respond to emerging safety information. Augmenting and enhancing the efficiency of those procedures would better serve the goal of promoting patient safety than instituting changes that may have an adverse impact on medical practice and patient adherence to medical advice from their physicians. For example, FDA's Advisory Committee procedures as well as the confidential communication between Sponsors and regulators as information becomes available are established processes that are well suited to obtain and evaluate potential safety concerns. These two processes permit a scientific discourse of the data to reach the appropriate recommendations. We believe that devoting the Agency's limited resources to the careful scientific consideration of data rather than to responding to questions and concerns about preliminary, untested information, better serves the public and the medical community.

The FDA currently has the ability and the remit to mandate changes in product distribution and labeling as a result of new safety information. The Agency has recently demonstrated its ability to mandate changes to product labels across entire classes of compounds (e.g. SSRIs, COX-2s and NSAIDs). These changes were instituted following public scientific debate, broad media coverage and widespread knowledge of the data covering the issues. It is unlikely that a Drug Watch website would have provided any additional insight or clarity to this debate but rather would have added to the confusion about FDA's position on the issues. These examples illustrate the use of FDA Advisory Committee Meetings as the appropriate forum to review and evaluate new safety information and to obtain the recommendation of leading experts regarding the need for further action. The lead time for scheduling and conducting the meetings has been criticized. We propose that the timelines for Committee consideration be shortened by reducing the lead times of submission and review of briefing packages. Improved communication processes could facilitate preparation for these public/private advisory committee sessions. The meetings have been called on an ad hoc basis in the past when an issue warrants. Finding ways to improve and speed this process would provide the necessary public scientific debate to reach a decision on the best path forward. Improvements in communication processes and the possibilities for enhanced electronic technologies would work together to significantly improve the process and timing of enacting a label change.

There are a number of labeling initiatives already underway which will improve dissemination of safety information to patients and physicians. However one issue remains unaddressed, i.e., dissemination of safety information from the date FDA approves the label change to the time when the label and packaging is revised by the Sponsor. This issue was raised at the Public Meeting on the Risk Management Concept Papers where pharmacists recommended that, should funds be made available, it would be possible to expedite dissemination of revised labels in a matter of days rather than weeks and months.

We believe a number of significant procedural issues also need to be addressed in association with the guidance. The interim period between posting the preliminary information and establishing the need to change the product label creates a significant legal and ethical dilemma for sponsors. Sponsors may be criticized and held responsible for failure to inform physicians of information that has not been properly investigated and reviewed. The situation is further confounded by the fact

that the sponsor did not have any input into the posting of the information on the FDA website, yet would most likely have to respond to questions from physicians and patients about the information posted. Moreover this problem is exacerbated by the fact that the current proposal contemplates notification of the sponsor immediately prior to posting of information in order to prevent interference by the sponsor that could bias the process. However, lack of adequate notification inhibits the Sponsor from being adequately prepared to respond to prescribers and patients as well as the media on the information posted.

Another procedural issue that needs to be addressed is the removal of a posting to the Drug Safety website and any remedial action to be taken to correct the negative impact created by preliminary and unsubstantiated information. Roche has had actual experience with the confusion generated by the posting of information on the forerunner of the Drug Watch page. Information obtained from various locations on the FDA website was posted on this preliminary version of Drug Watch. The mere fact that the information was now posted on this early version of Drug Watch generated numerous phone inquiries from concerned consumers and news media. They made the assumption, that this was new safety information that the company had not previously disclosed when in fact it was not new and was entirely consistent with the product label. If such confusion can be caused by the posting of evaluated and tested information, there should be serious concern with posting preliminary data without evaluation of that information and advice as to the impact of this information to current medical practice.

With respect to the establishment of the internal FDA DSOB, we believe this removes any contribution to the scientific discourse by both the Sponsor and independent experts in the area, thereby limiting the scientific debate and potentially prejudicing the decision making process. This could lead to a skewed debate as the expertise in any particular area would be limited to those within the structure of the DSOB. As currently proposed by FDA, input from outside the DSOB, whether from independent experts or the Sponsor, without regard for their knowledge of the issue, has been de facto declared suspect and/or unduly influencing the scientific decision-making process. While we understand the Agency's rationale for excluding this expertise from the decision-making process, we contend that excluding it from the discussion is a serious flaw in the proposed process.

Specific Comments:

In addition to the above general comments, we would like to provide specific feedback on the guidance document:

Line 22: The guidance notes that the "Drug Watch is intended to identify drugs which FDA is actively evaluating early safety signals." FDA needs to clearly define what constitutes an "early safety signal" (i.e. $PRR \geq X$, Number of reported events $\geq X$)

Line 31: The definition of serious side effects is unclear. Is this the standard definition (i.e. death, life threatening, hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect)?



Line 123: The guidance indicates that FDA intends to update this website when additional information or analyses become available. Clearly defined timelines are necessary.

Line 80 – 115: The categories and examples provided in the guidance do not clearly delineate risk information in a useful manner for the health care provider. Therefore, clear processes need to be defined with the evaluation criteria for each category of risk.

Conclusion:

The intent of the guidance and the website posting is to facilitate the transfer of drug safety information to healthcare professionals and patients. However, we believe the Agency’s proposal for “Drug Watch” has the potential to do more harm than good. There is significant risk that it will only add to the confusion of patients and could result in poor decision making based upon conjecture and innuendo, rather than best science and medical advice. Our view is that the Agency should focus additional effort on carefully considering its existing systems and possible enhancements or improvements that would satisfy the need for increased and faster information flow, rather than pressing forward with dissemination of untested, preliminary information. There is a potential for creating public confusion by posting limited and unadjudicated safety information. Patients should be able to obtain balanced information from their medical care providers about the risks and benefits of medications that allow them to make educated decisions. Patients do not have the education or training to evaluate incomplete or scientifically unsubstantiated information. We believe that the Agency should consider mechanisms to obtain additional public input to allow a full airing of all the issues and associated implications of the Drug Safety Website, including the potential for unintended consequences.

Respectfully Submitted,

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