



Michael D. Maves, MD, MBA, Executive Vice President, CEO

August 5, 2005

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

RE: Draft Guidance for Industry on the Food and Drug Administration's "Drug Watch" for Emerging Drug Safety Information [Docket No. 2005D-0062]

The American Medical Association (AMA) shares a common goal with the FDA to optimize the benefit/risk balance of drug therapy and to improve the safety of prescription drug products. To this end, the AMA appreciates the opportunity to offer the following comments on the Food and Drug Administration's (FDA) *Draft Guidance: FDA's "Drug Watch" for Emerging Drug Safety Information* (Federal Register, 2005;70:24606-24607).

General Comments

In its draft guidance, the FDA states:

"Our goal with the Drug Watch is to share emerging safety information before we have fully determined its significance or taken final regulatory action so that patients and healthcare professionals will have the most current information concerning the potential risks and benefits of a marketed drug product upon which to make individual treatment choices."

The FDA also provides examples of the types of emerging drug safety information that will appear on the Drug Watch and states that, because the Agency will still be evaluating the emerging safety information, it will accompany the information with a disclaimer, such as:

"This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this web page when additional information or analyses become available."

The AMA applauds the FDA's efforts to enhance transparency with regard to emerging safety information about specific prescription drug products, and we generally support the concept of a Drug Watch web page. The AMA believes the examples of emerging drug safety information, provided in the draft guidance and noted above, are reasonable examples of information that would be important to physicians. We also support the inclusion of the disclaimer.

Inclusion of Drug Products on the Drug Watch Webpage

In Section B of the draft guidance, the FDA discusses factors it will consider in determining whether a drug product is to be included on the Drug Watch web page. Specifically, the Agency intends to focus on:

- “whether new and emerging safety information could significantly affect prescribing decisions or how patients should be monitored;
- whether measures can be taken as a result of providing information that could help to prevent or mitigate harm; and
- whether an unapproved (off-label) use of the drug appears to pose a significant risk to patients.”

The AMA offers three comments on this section with specific emphasis on how drug products will be included on the Drug Watch web page.

First, we believe that any drug product for which FDA's preliminary analysis suggests new safety information is credible to warrant public dissemination should be posted on this web page. It should not be limited to the three situations listed above.

Second, while the AMA supports the inclusion of reasonable advice for prescribing a drug product based on FDA's preliminary analysis, we caution the FDA not to mandate or limit how the drug product can be prescribed without more definitive data that the drug product is, in fact, the cause of the adverse event.

Third, the AMA has strong concerns about FDA's decision to focus on off-label uses. Physicians want access to credible information when a drug product is ineffective for a particular indication, or when a new adverse event may be associated with the use of a drug product for a specific indication. Indeed, the AMA supports inclusion of this type of information on the Drug Watch web page. However, the AMA strenuously opposes the use of the Drug Watch web page as a mechanism for the FDA to more generally regulate off-label prescribing by physicians. For many years, the FDA has publicly stated that the Food, Drug and Cosmetic Act does not limit the manner in which a physician may use an FDA-approved drug, and the Agency has long recognized the appropriateness of off-label prescribing in medical practice. The AMA is hopeful that this continues to be the FDA's position especially since the need for off-label prescribing in providing optimal care for many patients is well documented.

The AMA generally supports a role for the Drug Safety Oversight Board in helping the FDA determine which drug products to include on the Drug Watch web page and when to remove a product. However, the AMA encourages the FDA to include practicing physicians among the consultants to this Oversight Board. The AMA believes the perspective of practicing physicians on how emerging drug safety information can be most effectively communicated to physicians would be of great value to both the Oversight Board and the Agency.

Drug Product Information Provided on the Drug Watch Web Site

Based on the information that is currently included on the “Drug Safety Initiative” section of the Center for Drug Evaluation and Research’s (CDER) web site, the AMA is concerned about the information to be provided on the Drug Watch web page. The AMA encourages the FDA to include the following information for a drug product that appears on the Drug Watch web page:

- FDA Alert. This would include a brief summary of the emerging safety concern.
- Data Summary. This would include a concise description of the evidence (e.g., from FDA’s MedWatch database) that led the FDA to conclude the emerging safety information is sufficiently credible to warrant inclusion on the Drug Watch web page.
- Recommendations. If the emerging safety problem warrants advice for physicians on potential changes in prescribing of the product, these should be provided in an advisory manner. Because the emerging safety information is based on a preliminary analysis, the FDA should not use language that either mandates or limits how a physician can prescribe the product.
- Disclaimer. Because the full significance of the emerging safety information is unknown and no final regulatory action has been taken, a disclaimer such as on lines 121-124 of the draft guidance should be included.
- Linkage. The information that appears for a drug product on the Drug Watch web page should be linked only to the professional labeling (i.e., the Package Insert, PI, or Prescribing Information) for that product.

Healthcare Professional/Patient Information Sheets and Links from the Web Site

The AMA has serious concerns with footnote 5 of the draft guidance, specifically the proposed “information sheets” for healthcare professionals and patients and about how the Drug Watch web site will be linked to a product’s Professional Labeling.

First, the AMA does not support the development of FDA’s proposed “Healthcare Professional Information Sheets.” To develop a separate set of “Healthcare Professional Information Sheets” is unnecessary and will result in redundant, and perhaps confusing, information for physicians. Instead, the AMA urges the FDA to invest its resources into developing a high quality Drug Watch web page that includes the information listed above, and to issue a Final Rule on a revised Package Insert consistent with its Proposed Rule of

December 22, 2000. Combined, these tools will be more useful and user-friendly to physicians.

Second, the AMA is concerned about linking information on the Drug Watch web page to "Patient Information Sheets," such as those currently found on CDER's "Drug Safety Initiative" web page. The AMA strongly supports the provision of adequate information to patients about the benefits and risks of drug products. The AMA also supports the public's right to be made aware of emerging safety information about a drug product. However, upon our review of the "Patient Information Sheets" on the current CDER web page, it is evident that there is a clear lack of fair balance between benefit and risk information in these "Patient Information Sheets."

The AMA does not believe this serves the best interests of patients or their physicians. From the patient perspective, these "Patient Information Sheets" send a clear message that the drug products have risks, but provide virtually no discussion of benefits. Moreover, it is not clear that the information, which is contained in these sheets under the heading "FDA Alert," is based on preliminary data where causality has not been proven. As currently written, these "Patient Information Sheets" may discourage patients from taking a potentially beneficial drug product.

In addition, the physician is put in the unenviable position of having to defend to his/her patient the choice of a drug product that has such a "Patient Information Sheet," even for drug safety information that is preliminary. This has the potential to add tension to the patient-physician relationship or, of more concern, result in the patient's refusal to take a medically necessary drug. Furthermore, these "Patient Information Sheets" may exacerbate the medical liability problem for physicians by providing plaintiffs' attorneys with documents that imply the drug products have many risks, but few or no benefits.

The AMA therefore recommends that drug products with emerging safety information on a Drug Watch web page not be linked to "Patient Information Sheets," as they currently appear on the CDER web site. As noted above, the AMA suggests that the only linkage from a drug product on the Drug Watch web page be to the Package Insert. However, linkage to patient information based on the Package Insert may be acceptable when written in lay language, and appropriately balanced for benefits and risks. The (Keystone) *Action Plan for the Provision of Useful Prescription Medicine Information* (per P.L. 104-180), accepted by the Secretary of Health and Human Services in January 1997, may serve as a useful guide to develop written patient information.

The AMA appreciates the opportunity to offer these comments and recommendations to the FDA on its proposed Drug Watch web page. We are hopeful that the FDA agrees with the AMA's recommendations to make this a useful web page to communicate emerging drug safety problems. We would be pleased to discuss this matter further.

Sincerely,



Michael D. Maves, MD, MBA