



March 31, 2009

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

Re: Docket No. FDA-2008-N-0038, Risk Communication Advisory Committee Meeting, February 26-February 27, 2009.

Dear Sir/Madam:

The American Society of Health-System Pharmacists (ASHP) is pleased to submit written comments pertaining to prescription drug information currently available to patients in the form of Medication Guides, Patient Package Inserts (PPIs), and Consumer Medication Information (CMI). As the national professional association representing over 35,000 pharmacists who practice in hospitals and health systems, ASHP can offer unique and vital feedback on this important health-care issue. Pharmacists in hospitals and health systems are experts in medication use who serve on interdisciplinary patient-care teams. They work with physicians, nurses, and other health-care professionals to ensure that medicines are used safely and effectively.

ASHP was pleased to participate in the Risk Communication Advisory Committee (Advisory Committee) Meeting held on February 26 and February 27, 2009, when the Society made an oral presentation to the Advisory Committee during the Open Public Hearing section of the meeting. The following comments expand and elaborate on those oral comments. ASHP appreciates FDA's willingness to consider our recommendations as it considers appropriate next steps to improve the communication of patient information regarding prescription drugs.

ASHP promotes safe medication use by publishing federally recognized, evidence-based drug information. The Society publishes best practices guidance documents, participates in key national safety and quality initiatives, and has published CMI for over 30 years. Our CMI is widely accessed via the National Library of Medicine's MedlinePlus consumer website, ConsumerReportsHealth.org website, and ASHP's safemedication.com website. The Society integrates Medication Guide (MedGuide) and Black Box Warning safety information into its CMI, with hyper-links to the full text of

the MedGuide embedded in the electronic CMI and URLs and patient access instructions included in the print versions.

2008 Final Report

In 1995, the Food and Drug Administration (FDA) proposed a regulation to set and assess specific goals regarding the distribution and quality of medication information provided to consumers. Specific goals of the regulation included a target that by the year 2000, 75% and by 2006, 95% of new prescriptions dispensed would include “useful” written information for patients.

The 2008 Final Report, *Expert and Consumer Evaluation of Consumer Medication Information* (Final Report), assessed whether the 2006 goal that 95% of people receiving new prescriptions should receive “useful” written patient information with their prescriptions was being met according to criteria that purportedly were contained in FDA’s 2006 Guidance on Useful Written Consumer Medication Information (CMI). While the Final Report found that the majority of community pharmacies provided computer generated CMI, the length and format of the CMI and the percent of critical content items covered varied considerably from pharmacy to pharmacy.

However, the Final Report did not establish the root cause of adherence issues, since the study did not perform a separate evaluation of the original content provided by the source publisher versus the content distributed downstream at the point of dispensing. Therefore, conclusions that can be drawn from the Final Report are incomplete, since FDA did not address important study design flaws and associated concerns raised by ASHP relating to the earlier 2001 evaluation. Even without this separate evaluation of the original content, there was a strong indication in the 2008 evaluation that problems noted in the Final Report lie at the point of distribution, rather than with the content provided by the CMI source publishers. For example, the Final Report showed the elimination of substantial content from the distributed information at the point of service, thus demonstrating a failure to adopt best practices for formatting and legibility at the point of dispensing.

Additionally, the 2008 Final Report included a substantial number of subcriteria that were not defined by the recommendations included in the report titled *Action Plan for the Provision of Useful Prescription Medicine Information* (the Keystone Criteria) or FDA’s July 2006 Guidance on Useful Written CMI (Guidance). Therefore, in 2008, CMI was evaluated using a higher standard than is required under existing guidelines. ASHP raised similar concerns about the 2001 assessment, which were presented in face-to-face meetings with the primary investigator and FDA personnel, and submitted a detailed analysis showing that only 50–65% of the subcriteria could be directly attributed to labeling and were explicitly required by the Keystone Criteria.

For example, the lower adherence to subcriteria from the Guidance, under *Criterion 1: Drug Name, Indications for Use, and How to Monitor for Improvement* (actually assessed in 2008 under Criterion 3), relative to the previous evaluation, was an indicator of the application of a standard that exceeded the Keystone Criteria and the 2006 Guidance. The FDA Guidance states: "Information regarding how to monitor the effectiveness of the treatment by correctly interpreting *physical reactions* to the medicine, if this is in the package inserts." Using lisinopril as an example, 47% of the subcriteria (8/17) contained specific advice about the frequency and specific type of lab tests, none of which were related to *physical reactions* as specified in the FDA guidance. While information on the frequency and specific type of lab tests may be useful to communicate to the patient, this information is not included in the standard established by the FDA Guidance. That is why less than 20% of CMI adhered to specific subcriteria on frequency of laboratory tests and actions to take. For clarity, it should be noted that the authors of the Final Report moved provision of such information from Criterion 1 (as specified in the FDA guidance) to Criterion 3 without explanation. ASHP will submit more detailed comments about the 2008 Final Report at a later date as specified in the docket.

Study conclusions presented to the Risk Communication Advisory Committee during the February meeting were flawed due to this issue and other study design problems, which calls into question the resulting recommendations of the Advisory Committee concerning the failure of private-sector CMI.

Private Sector Publishers of CMI

The private publishing sector has invested heavily to improve CMI as a result of both the findings from the 2001 study, which evaluated CMI obtained from pharmacies for four commonly prescribed medications, and the subsequent 2006 FDA Guidance. In addition, the CMI publishers have implemented an extensive, well-established infrastructure for timely revision and distribution of the content to consumers. In order to fully utilize this existing, well-developed system and infrastructure, ASHP encourages FDA to create a stronger public-private partnership moving forward. For example, FDA might consider establishing a certification process for private-sector publishers overseen by a neutral party such as the United States Pharmacopeia (USP), or by FDA itself. ASHP also recommends that FDA conduct well-designed research to establish the effect of CMI on patient adherence, behavior, and outcomes before implementing any major changes to the currently recommended language and format for useful CMI.

If changes are implemented, ASHP recommends that specific criteria and subcriteria be clearly documented, with examples of style and wording for a wide range of medication and product types (e.g., those with black box warnings and other significant risk factors, various routes, various disease state severities and durations such as acute versus chronic illnesses). This information should be updated periodically as other issues arise or are addressed by FDA. Any future assessments of written CMI, including possible

certification methods, should be based on explicit standards as stated in FDA guidances and associated documentation. (See also Recommendation 4 below.)

Drug Facts Box Format

If FDA discontinues the use of private-sector CMI and implements a system where the pharmaceutical companies develop the CMI and FDA then approves the documents, patients could potentially be without any regularly distributed risk information for many years, since FDA would be tasked with reviewing and approving thousands of CMI documents. For economic reasons, the private-sector companies that currently produce CMI would be unlikely to maintain the resources needed to continue to update, enhance, and distribute their CMI through existing channels while the new process is being implemented, potentially resulting in a major void in risk communication to consumers.

ASHP recommends that FDA draft a regulation that involves drug manufacturers in developing a new Drug Facts Box as the required summary format (described by the Advisory Committee as level 1) for CMI. FDA should continue its public-private partnership with the CMI publishers for the more detailed information (described by the Advisory Committee as level 2) that many consumers will require, since the Drug Facts Box would provide only limited risk-benefit information, albeit information that is considered clinically important for prescribing purposes. This two-level content model would focus on the development of a regulated Drug Facts Box as the primary level, with more detailed information provided by the private sector publishers as the secondary level. By following this approach, the existing infrastructure would remain in place as FDA works to approve the Drug Facts Box information for new products over the years. In addition, FDA could work through a public-private partnership to further enhance the usefulness of the secondary level CMI, as guided by well-designed research that focuses on patient needs.

Multiple Sources of Consumer Risk Information

Currently, there are multiple sources of consumer risk information, including CMI, MedGuides, Patient Package Inserts (PPI), and FDA alerts, potentially resulting in consumer confusion. ASHP believes that educating consumers about the safety issues covered by Medication Guides is important. However, the Society questions whether Medication Guides as they are currently written and distributed are valuable tools for counseling patients about drugs with serious risks, since evidence of their usefulness has not been established through adequate, well-designed research. Furthermore, MedGuides focus only on the risks of a drug. There is little, if any balance regarding the benefits of treatment.

Despite the general requirements under the MedGuide regulations, there is highly variable content between MedGuides, and the Guides are far too long. In its December 1, 1998 Final Rule on Medication Guide Requirements, FDA stated: "FDA is concerned

that, if unrestrained, lengthy information could result in unnecessary or even dangerous barriers to the effective communication of important concepts. Therefore, the agency will establish a two-page limit as a goal for the communication of the essential information to be included in Medication Guides.” This two-page limit has not been enforced by FDA.

One-Document Solution

ASHP supports a one-document solution for the detailed information, combining both CMI and MedGuide safety and risk information. However, even if FDA were to follow its own guidance and substantially reduce the length of MedGuides, it is unlikely that the proposed Drug Facts Box could adequately incorporate the risk/benefit information in the context of space limitations and other safety and risk information about the medication. Therefore, ASHP recommends that MedGuide information be incorporated in the second-level, more detailed CMI, but in summarized form as is currently done by the private publisher sector.

Although the suggestion in the Citizen’s Petition to moved to a “one document solution” to provide consumer medication information is a positive step for consumers, the focus on the use of the Highlights section of the prescribing information presents significant concerns. The Highlights section was developed to be a summary document to “direct the practitioner to the more detailed information in the PI.” Therefore, it was not meant to be a comprehensive, stand-alone document to convey information to the consumer about the use of prescription medications. Even if the current wording were consumerized as suggested by the Citizen’s Petition, the content is not consumer focused as it often contains prescribing and administration information that is directed towards the prescriber. Little, if any, of the Highlights section contains information directing patients as to what they should do if adverse events occur or at what point the prescriber should be notified. The suggestion by the petitioners to also use the information for direct to consumer advertisements reinforces these concerns as this information is only required by Federal Law to contain effectiveness and risk information and not the full spectrum of information needed by consumers to use their medications safely and effectively.

Recommendations

In addition to the specific recommendations included above, ASHP makes the following more general recommendations as FDA examines the issue of prescription drug information available to patients:

1. FDA should conduct well-designed research to determine optimal content and format of CMI. Research should be patient/consumer-centered.
2. For the comprehensive format of CMI, the goal should be a single, comprehensible document. FDA should examine the use of existing CMI integrated with the relevant MedGuide versus the use of stand-alone documents.

- Additional prototypes should be tested as necessary. ASHP strongly cautions that the “Highlights” section of the professional labeling is not designed to serve as the basis of an integrated document.
3. FDA should make use of the existing, well-established infrastructure for content development and deployment, which currently has been assessed with a 95% adherence rate for patients receiving written CMI. Other recent deployments, such as FDA’s original method for distributing MedGuides, have not demonstrated this level of compliance. In fact, a 2005 FDA survey of more than 5000 pharmacies showed that only 30% of respondents knew that distribution of MedGuides was a federal requirement. FDA resisted early efforts by private sector publishers and downstream distributors of CMI to utilize existing distribution channels to ensure high patient delivery adherence with MedGuides.
 4. FDA should ensure that guidance documents are as specifically detailed as any assessment criteria used to evaluate CMI, including full documentation by researchers of the source information for content and how each subcriterion meets *explicit requirements* of the standards. The professional labeling (package insert, PI) should be the minimum standard, and subcriteria that do not meet explicit requirements as defined in the standards as well as content from other sources should be considered enhancements that exceed the standard. Since FDA did not enforce such an interpretation by researchers conducting its 2001 and 2008 evaluation, the validity of the evaluations and the resultant recommendations are greatly limited. ASHP previously recommended that the criteria be published for public comment following sampling of materials to be evaluated as one possible mechanism to ensure that expert panels utilize the intended standards.
 5. FDA should fully engage stakeholders in the process.
 6. FDA should clearly establish what is most important to communicate to consumers and how. Risk/benefit, safety information, and instructions on how to use a medication should all be considered.
 7. FDA should identify the best times to communicate risk/benefit, safety information, and instructions on medication use to consumer, including at the time of prescription, at first prescription refill, and/or at each prescription refill.
 8. FDA should ensure the downstream adoption of optimal content, language, and format by improving stakeholder and boards of pharmacy engagement.
 9. FDA should fully consider the economic impact on content publishers, pharmacy/health information systems vendors, and pharmacies, and develop a realistic time-frame for the adoption of any change.
 10. Any change should be implemented only with sound evidence to support the change.

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The Society appreciates this opportunity to present its written comments relating to the Risk Communication Advisory Committee meeting. Feel free to contact me if you have any questions regarding our comments. I can be reached by telephone at 301-664-8702, or by e-mail at jcoffey@ashp.org.

Sincerely,

A handwritten signature in cursive script that reads "Justine Coffey".

Justine Coffey, JD, LLM
Director, Federal Regulatory Affairs