

July 25, 2005

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



American Society of
Health-System Pharmacists*

7272 Wisconsin Avenue
Bethesda, Maryland 20814
301-657-3000
Fax: 301-652-8278
www.ashp.org

Docket No. 2005D- 0169

To Whom It May Concern:

The American Society of Health-System Pharmacists (ASHP) is pleased to respond to the Food and Drug Administration's (FDA's) May 26, 2005, request for comments on its "Draft Guidance on Useful Written Consumer Medication Information (CMI)." ASHP is the 30,000-member national professional and scientific association that represents pharmacists who practice in hospitals, health maintenance organizations, long-term-care facilities, and other components of health systems.

ASHP believes that the mission of pharmacists is to help people make the best use of medicines. Assisting pharmacists in fulfilling this mission is ASHP's primary objective. Components of the Society's efforts in assisting pharmacists in this regard include position and guidance documents for best practices such as those on pharmacist-assisted patient education and counseling (first published in 1975), extensive publishing activities with a strong focus on professional and patient drug information, and educational programs. ASHP has long held that private sector publishers, including professional associations, must play an important role in the creation and dissemination of useful medicine information.

As a private-sector publisher, ASHP represents the perspective of a scientific, nonprofit publisher of evidence-based drug information. We have published *AHFS Drug Information* (originally called the *American Hospital Formulary Service*) since 1959. The authority of *AHFS Drug Information* includes federal recognition through legislation and regulation as an "official" compendium for information on medically accepted uses of drugs. As a well-respected publisher of evidence-based drug information, ASHP also has applied this expertise for almost 30 years in publishing high-quality drug information for consumers.

With the release in 1978 of the first edition of the "Medication Teaching Manual: A Guide for Patient Counseling," ASHP became one of the first private-sector organizations to publish medication monographs intended for educating patients. This manual was developed by an advisory committee that ASHP formed cooperatively with the American Hospital Association (AHA) and US Department of Health, Education, and Welfare's Bureau of Health Education. ASHP is a past recipient of an award of excellence for

consumer education materials from FDA and the National Coalition for Consumer Education (NCCE).

ASHP also was one of the first (perhaps the first) publishers to address the guidelines of Department of Health and Human Service's (DHHS) 1996 Action Plan for the Provision of Useful Prescription Medicine Information ("Keystone guidelines"). ASHP's quick response to the Action Plan resulted in a major revision and reformatting in 1997–1998 of its "Medication Teaching Manual" and associated consumer medication information (CMI) resources. A variety of products and services currently are created from ASHP's master database of CMI (MedMaster database), including its MedTeach software used by healthcare professionals to provide customized patient monographs, the National Library of Medicine's MedlinePlus consumer website, the Consumers Union's Consumer Reports Medical Guide website, and others. The MedMaster database also serves as the basis for ASHP's widely acclaimed safemedication.com consumer website. In fact, ASHP's monographs often have been used as models of useful CMI, including by Dr. Bonnie L. Svarstad¹ (Principal Investigator of FDA's 2001 Evaluation of Written Prescription Information Provided in Community Pharmacies).

In large part, it was ASHP's criticism of FDA's 2001 assessment by Dr. Svarstad that led to FDA's development of the draft guidance. Beginning with public comments in July 2002 and 2003 and continuing with stakeholder meetings organized by the National Coalition of Patient Information and Education (NCPIE) that included FDA, ASHP has pointed out methodological problems with the study design, particularly the inclusion of a substantial proportion of specific criteria for determining usefulness that were not supportable from FDA-approved labeling and/or the Action Plan. In fact, only about 50–65% of the criteria used in the Svarstad study could be directly attributed to labeling and were explicitly required by the Action Plan as part of ASHP's analysis (attached). At the June 17, 2004 meeting that was convened by FDA with the assistance of NCPIE, both Dr. Svarstad and FDA acknowledged such methodological problems and agreed that some guidance should be developed to ensure a fairer, more objective evaluation in 2007 that was in better keeping with the language and intent of the original Action Plan.

We find that the draft guidance follows Chapter 3, of the Keystone "Action Plan for the Provision of Useful Prescription Medicine Information," but we are not convinced that it offers practical advice beyond Keystone Chapter 3. In fact, in several key ways, we find that the draft guidance actually exceeds the language and intent of the Actions Plan and would create new burdens for publishers that were not previously embodied in the guidance. As previously noted, ASHP's monographs have often been used as models for useful CMI and have not been the focus of recent criticism by FDA or others. Despite this, however, substantial resources likely would need to be devoted even by ASHP if the draft FDA guidance were to be adopted. In particular, ASHP is concerned with FDA's language about the inclusion of *all* precautions to meet criterion 4 of useful CMI. This

¹ Svarstad BL (University of Wisconsin-Madison School of Pharmacy, Madison, WI) : Personal communication and request for permission to distribute ASHP MedTeach reprints; 2004 Jun 10. Svarstad BL: Comments (personal observations); FDA/CMI Criteria Committee Meeting, Rockville, MD; 2004 Jun 17.

exceeds the language of the Action Plan, which is limited only to “applicable” precautions, with additional language stating that precautions “are encouraged in serious situations.” Therefore, ASHP sees no basis in the Action Plan for FDA’s current interpretation stated in the draft guidance (line 263). If finalized, this new standard would greatly raise the bar and require considerable resources for ASHP to ensure compliance, something that likely could not be accomplished in time for FDA’s next scheduled evaluation of written CMI.

Some specific points that we have identified are as follows:

Lines 20-22 – Variety of CMI

The introduction to the draft guidance states that “CMI is written information about prescription drugs developed by organizations or individuals other than a drug’s manufacturer that is intended for distribution to consumers at the time of drug dispensing.” ASHP recommends that mail-order pharmacies be included in the mix of outpatient pharmacies that are included in the 2007 evaluation, since a growing number of such prescriptions are now dispensed from such settings.

In addition, FDA should recognize that consumers may also access this type of information at times other than receiving the prescription or refills via Internet sites or directly accessible computer programs. While not included in the scope of the Action Plan, future research on the usefulness of such information is encouraged since consumers increasingly are accessing information independently via the Internet, and very few standards for health information in general currently are being applied.

Line 114 – Background

FDA should discontinue specific reference to the 50% average *usefulness* included in Dr. Svastad’s original study. As described earlier, both the principal investigator (Dr. Svarstad) and FDA have acknowledged that the specific criteria employed in this study exceeded the requirements for determining usefulness as outlined in the Action Plan. The Action Plan clearly states and this draft guidance acknowledges that the minimum standard for establishing compliance is the FDA-approved labeling, and many criteria included in the 2001 evaluation had no basis in labeling but instead merely represented the opinions of a clinical consultant, the investigators, and panelists. While such criteria may in some cases represent good information to share with consumers, they should not have been used to establish minimum criteria for determining usefulness in the 2001 evaluation of compliance of CMI with the Action Plan.

Lines 127-129 – Minimum Characteristics

FDA considers meeting the criteria and components of the Keystone Action Plan as the “minimum” appropriate characteristics of useful CMI. Since the draft guidance

does not indicate what would be an improvement over Keystone, it is hard to say what this means and whether exceeding the minimum standard could count positively in the overall assessment of usefulness (e.g., an “exceeds” determination).

Lines 144-147 -- Approved Package Insert (PI)

FDA is emphatic here, as well as in lines 333-34, that the FDA-approved PI must serve as the source document for the information in the CMI, or the information in the CMI will not be considered “useful.” There is often valuable patient or consumer information available from the manufacturer’s website or by phone contact with the manufacturer. Additionally, important information from references is useful to describe a drug’s mechanism of action and disease state information. The PI may serve as a good baseline, but additional information will provide more comprehensive information for the layperson without a background in the disease state.

In some cases, more recent well-substantiated evidence actually may refute information that continues to appear in labeling. Inclusion of such information may be in the consumer’s best interest in weighing the risks and benefits of therapy. For example, warnings about cardiac risk in the labeling of sulfonylurea antidiabetic agents are based in large part on old, controversial UGDP data, which more recent UKPD data could not confirm. Therefore, FDA’s guidance should allow inclusion of information outside labeling that attempts to provide a balance and it should not negatively score against the evaluation of usefulness. Likewise, acknowledging the widely recognized (e.g., by the American Heart Association and American Diabetes Association) benefits of beta-blockers in diabetics despite only precautionary information appearing in labeling represents another example of not negatively scoring CMI in the interest of providing balance

Footnote (8) for these lines and the original Action Plan state that customized CMI can contain patient-specific information that is not included in the FDA-approved labeling. However, new in FDA’s draft guidance is the recommendation that the source of such information be included in the actual CMI. It seems impractical to include such referencing in the information intended for use by consumers, and complying with such a change in interpretation of the Action Plan at this late date would place considerable burden on publishers that could jeopardize any possibility of meeting the 2007 goals. Maintaining documentation as archival records rather than actually including such documentation in CMI intended for consumer use has long been the publishing standard for CMI developed both by the public and private sectors.

FDA also states that the most recent labeling must be reflected in CMI. Not even FDA’s own websites nor those of the manufacturers routinely reflect the most recent labeling. In addition, there always will be some lag time between publication of revised labeling and incorporation in any derived document,

including CMI. Therefore, some reasonable alternative time frame (e.g., current within the past six months) should be acknowledged as should the modifier “readily accessible” for the aforementioned reasons.

Lines 181-183 – Drug Names

The draft guidance and the Action Plan require the phonetic spelling (pronunciation) of a drug’s established name, which has long been interpreted to mean generic (nonproprietary) name. “The USP Dictionary of USAN and International Drug Names” provides pronunciation for official US titles. While FDA *recommends* in the draft guidance that pronunciations also be included for brand names, there is no official pronunciation for these names, and contacting each manufacturer to establish such pronunciations would be impractical. In addition, some drugs literally have hundreds of brand names, adding greatly to the impracticality of this recommendation. It was never the intent of the Action Plan that either all brand names or their pronunciations be included in CMI.

Currently, USAN and USP serve as the source of established names in the US. Footnote 9 states that the Action Plan was incorrect in its interpretation that not all drugs have established names. It has been ASHP’s experience that the established name for some drugs is not always apparent. Therefore, what authoritative source should publishers reference when there is no apparent established “compendial” (i.e., USP or USAN) name? Also, can USP’s PEN’s be considered established, convenient names when referring to certain common combinations such as co-trimoxazole (assuming the individual components are also described)?

Line 185 – FDA-Approved Indications

It is surprising that "all" FDA-approved indications in the PI need to be in the CMI. We are not aware that database publishers do that currently. *AHFS-DI* includes all indications, and we attempt to keep up with new indications.

Line 199 – Contraindications

The FDA draft guidance states that "all" contraindications must be included in the CMI. This may be appropriate, but some contraindications may some only apply as signals for the prescriber. Patients are not always involved in prescribing or assessing if they have a certain disease state, so they only appear as, “tell your doctor if you have....”

Line 219 – CMI as a Stand-Alone Document

It is unclear what FDA means when the agency states in the draft guidance that the CMI must be a stand-alone document. Does all the information on other prescription vial labels (e.g., directions for use) have to be in the CMI as well? It is an unknown whether software vendors/pharmacies can satisfy this requirement, as

it is impossible to know what dosage form, strength, or frequency of administration the doctor will prescribe. This information would have to be added at the point of dispensing.

Line 240 – Missed Dose

The draft guidance states that information about what patients can do if they miss a scheduled dose must be in the CMI if it is in the PI. If missed dose information is not in the PI, does that mean it cannot be included in the CMI? We suspect that many medication information publishers have such information. We consider this information to be important to patients. Additionally, missed dose information is not in most PIs; it is often only in patient information – i.e., MedGuides -- or web-based FAQ information.

Line 261 -- Boxed Warnings

Why does the FDA draft guidance lump the "Black Box Warnings" with other Warnings/Precautions, even though the guidance does say it must be prominently displayed? The Keystone Action Plan lists boxed warnings as the second item in its "components of information" section, right after the drug name. The first four items were listed discretely in the Action Plan and were identified to be always written in that order.

Line 263 – Precautions

The draft guidance states that the CMI must "include all information stated in the PI regarding what precautions the patient should take while using the drug." The word "all" again strikes us as being quite a rigorous requirement. There may be precautions that may be relevant to the prescriber only and not necessarily for the patient. Based on our reading of the draft guidance, these would still need to be in the CMI. Some prescriber precautions can be "translated" to apply to patient information (e.g., "tell your doctor"), but the requirement in the guidance seems to be too stringent.

Lines 276-278 -- Behavioral Instructions not in the PI

This is the only place in the draft guidance where FDA seems to let a provider of CMI deviate from the PI, i.e., to specify a behavior to be avoided if implied by a warning/precaution (but not stated) in the PI. On the other hand, FDA does not appear to allow for inclusion of risk information in a CMI that is well documented in the literature, but does not yet appear in the PI.

Lines 284-287 – Risks to the Fetus or Infant

It is understandable that the risks for pregnancy, labor, or breast feeding be communicated to the patient. It is not clear however, why the statement "It is not

known if the medicine will affect your baby” is suggested. There may be further information available to the clinician that could be used to evaluate continued use of the drug in the patient. It is better to say “if you become pregnant while taking this medication, contact your doctor” rather than have the patient arbitrarily discontinue the medication because she is informed that “there is no information available.”

Lines 297-299 – Adverse Drug Reactions

Here, the draft guidance provides some useful and new advice, stating that the CMI should list the symptoms of 5-9 most frequent ADRs. On a cautionary note, FDA should be aware that some important AE information may occur less frequently (e.g., hypersensitivity reactions) and should be included in the CMI, but may not specifically be listed in the PI.

Line 349 -- Level of Understanding

The draft guidance states that the CMI “should be written in wording that is understandable and suggests using a validated readability instrument. The FDA should include specific examples of validated readability instruments that it considers acceptable?

Lines 391-404 – Suggested Order of CMI Components

FDA gives its favored headings/order, but says this is not the only appropriate headings/order, but says little more. The guidance should state that this preferred order is different from the order in the Keystone Action Plan, and refer to examples of CMI in Appendix G of the Action Plan.

For more than 60 years, ASHP has helped pharmacists and pharmacy technicians who practice in hospitals and health systems improve medication use and enhance patient safety, and we appreciate the opportunity to present comments on this important patient care issue. We believe that the FDA, as it finalizes its guidance for useful CMI, should work with organizations such as ours in order to create a more effective document than the one issued for comment. 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 gstein@ashp.org.

Sincerely,

Gary C. Stein
Director of Federal Regulatory Affairs

Attachment