

**July 25, 2005**

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

**Re: Docket No. 2005D-0169 (70 Fed. Reg. 30467, May 26, 2005)  
Comments on FDA's "Draft Guidance – Useful Written Consumer  
Medication Information (CMI)"**

First DataBank, Inc. ("First DataBank") is a leading publisher of drug information. As part of First DataBank's product portfolio, First DataBank develops and publishes consumer medication information ("CMI") on over two thousand pharmaceutical products. In addition, as a formal member of the National Council on Patient Information and Education (NCPIE) since 2003, First DataBank has been involved in and has supported the development of private-sector initiatives to improve communication regarding prescription medicines to consumers. Prior to 2003, First DataBank's professional staff also participated actively in NCPIE programs.

For these reasons, First DataBank is keenly interested in FDA's recommendations with respect to the content of useful written CMI as published by FDA on May 26, 2005. Our general and specific comments with respect to the draft guidance are as follows:

**General Comments:**

**I. FDA should provide adequate time for implementation of recommendations in the anticipated official CMI guidance.**

On August 6, 1996, Public Law 104-180 was enacted. The legislation adopted the following goals: (i) the distribution of useful written CMI to 75 percent of individuals receiving new prescriptions by the year 2000; and (ii) the distribution of useful written CMI to 95 percent of individuals receiving new prescriptions by the year 2006. The legislation established a process by which interested private sector stakeholders would develop an action plan in order to achieve the goals set forth in such legislation.

Such an action plan, entitled "Action Plan for the Provision of Useful Prescription Medication Information" (aka the "Keystone Guidelines" or "KG"), was developed by a steering committee facilitated by the Keystone Center in 1996. It consists of broad, generalized guidelines for the development of useful CMI by private sector drug information publishers and is not directed toward pharmaceutical manufacturers.

Significant (and appropriate) latitude was granted within the KG with respect to clinical decision-making on the part of healthcare professionals authoring CMI.

Former Department of Health and Human Services (HHS) Secretary Donna E. Shalala wrote on January 13, 1997, in her formal acceptance letter of the KG, the following:

*"I strongly believe that it will take a concerted effort by all involved to achieve the Plan's goals. The Department (HHS/FDA) stands ready to assist in that effort. FDA will continue its periodic efforts to determine the quantity of information provided and, as the Plan also requests, provide general reviews of product quality. This will give the private sector a sense of its progress in meeting the goals of the statute, without interfering with the private sector efforts."*

In order to provide "general reviews of product quality" as the Former Secretary stipulated, FDA guidance on this subject would have been appropriate and necessary back in early 1997, with updates or any new input from FDA as they occurred over time. Moreover, during the FDA Risk Management Advisory Committee meeting of June 2002, among the recommendations adopted was that FDA should maintain a structured oversight and guidance effort in the private sector CMI initiative. This constituted another official call for an FDA guidance document with respect to its interpretation of the KG and its recommendations as to what constitutes useful CMI. Even at that relatively late date in 2002, CMI developers and other stakeholders could have effectively utilized such a guidance document as a basis to review and revise thousands of CMI documents as necessary by the 2006 deadline. Yet no such guidance document arose from that Advisory Committee meeting.

Despite the clear necessity of specific recommendations by FDA as to what constitutes useful CMI after the development of the KG in 1996, FDA only now proposes to address such recommendations in this draft guidance, almost ten years later. It is now four years since FDA commissioned the National Association of Boards of Pharmacy (NABP) to conduct the first formal survey on CMI to determine whether the first goal set forth in Public Law 104-180 was met (the "2001 Survey"), and a mere one and a half years before the next survey will be conducted in 2006 to determine whether the second goal set forth in Public Law 104-180 is met (the "2006 Survey").

FDA states in this draft guidance that "[t]his guidance is intended to assist developers of CMI in meeting the 2006 goal by providing specific recommendations regarding the minimum appropriate characteristics of useful CMI." Given the thousands of CMI documents that each database developer maintains (with well over one million words per database), it is inherently unfair for FDA to propose recommendations at such a late date, especially if some of those recommendations are not consistent with the intent of the KG. The implementation of any such new recommendations by the 2006 deadline would be extremely burdensome on private sector CMI developers.

## **II. Draft guidance is of limited usefulness in assisting private sector to meet 2006 goal.**

A very detailed, concrete, objective CMI survey instrument is necessary in connection with the 2006 Survey. Survey criteria and sub-criteria must be consistent with the KG, and must be highly drug-specific in most cases. In order to bridge the large gap between the broad, general KG and the highly-detailed, concrete survey instrument, FDA guidance that would “operationalize” the KG, or serve as the bridge between the KG and the survey instrument, is necessary to assist CMI developers and any other interested stakeholders to assess whether the CMI that they have developed is useful and whether they are on track to meet the 2006 goal. However, much of FDA’s draft guidance merely restates the criteria set forth in the KG without making such criteria more concrete and practical/operable. Further, the late date of draft guidance presentation is an issue, as discussed in part I above.

### **III. FDA should establish an adequate feedback process with private sector CMI developers.**

Another key component necessary for the implementation of Public Law 104-180 and the KG is the establishment of a functional feedback/dialogue loop between the FDA and the private sector stakeholders. Former HHS Secretary Shalala’s 1997 letter (quoted previously) indicated the need for such feedback when she discussed *FDA “general (informal) reviews of (private CMI) product quality”* and *“giving the private sector a sense of its progress in meeting the goals...”* As noted above, The 2002 FDA Advisory Committee meeting recommendations also directly supported a feedback process by FDA.

This feedback process logically could have been established many years ago through the National Council on Patient Information and Education (NCPIE). In fact, in December 2002, FDA encouraged NCPIE to step forward and serve as a catalyst and convener for private sector stakeholders, many of which are NCPIE members. At that time, assurances were provided by FDA that the agency would work closely with NCPIE and stakeholders by providing, for example, technical advice, and feedback for such efforts moving forward.

Virtually all interactions with FDA related to private sector CMI have been initiated by NCPIE or its members since 1997. For example, the CMI Criteria Committee of NCPIE, in connection with its CMI Initiative, completed a “Guide for Determining the Usefulness of Consumer Medicine Information (CMI)” (the “NCPIE Assessment Guide”) in the summer of 2004, in the continued absence of any such feedback or advice related to operationalizing the KG in accordance with FDA’s planned final assessment. The NCPIE Assessment Guide was submitted to FDA for comment and feedback, with the expectation that FDA would have final editorial control. It was also anticipated that the NCPIE Assessment Guide would be internally reviewed by FDA as the agency prepared what private sector groups awaited for nearly six months between March 2004 and August 2004 as a “Points to Consider” document on CMI from FDA.

NOTE: The “Points to Consider” document would serve the same purpose as the NCPIE Assessment Guide (or the current FDA draft Guidance).

Subsequently, FDA informed stakeholders that it had decided instead to issue a draft guidance on CMI instead of the “Points to Consider” document. This decision then precluded FDA from commenting on the NCPIE Assessment Guide until such guidance was issued, created a lag time of nine months during which no meaningful communication about operational issues could be discussed with the agency.

Without feedback from FDA on the NCPIE Assessment Guide, NCPIE has not distributed it to key stakeholders, including publishers, system vendors, chain, independent, mail order and other pharmacy/pharmacist organizations, and regulators, including NABP and State Boards of Pharmacy. The NCPIE Assessment Guide content is practical, clinically sound information which would be useful to CMI developers and other stakeholders. First DataBank would welcome an expeditious FDA review and comments on the NCPIE Assessment Guide, given its valuable, practical clinical content, and would encourage FDA to look to the NCPIE Assessment Guide in preparing its final guidance on useful written CMI. However, there is still the issue of the late date of the FDA draft guidance, as noted in part I above.

#### **Specific Comments:**

*Line 114:* The 50% usefulness figure quoted for private CMI is a reference to the 2001 Survey. A number of the sub-criteria developed for that 2001 Survey have been shown to be subjective/arbitrary in nature (e.g., source information not being present in professional labeling) based on a detailed analysis by the American Society of Health-System Pharmacists (ASHP). A summary of results is available upon request ([Nicholas\\_ratto@firstdatabank.com](mailto:Nicholas_ratto@firstdatabank.com)), or consult the ASHP comments on this docket for a full description.

#### **Criterion 1**

*Line 172:* While “monitoring for improvement” is a reasonable clinical consideration for CMI, the KG do not mention this parameter. Further, the package insert (“PI”) does not routinely address such monitoring. The draft Guidance should adhere to the KG for consistency.

*Lines 181—183:* The “phonetic spelling of the brand name” recommendation is not part of the KG.

*Lines 185—187:* Stipulating inclusion of all indications from the PI is too proscriptive and not the intent of the KG. The KG do not stipulate inclusion of all approved indications. From a patient care standpoint, sometimes not all approved indications should be listed. For example, if a drug is indicated for 5 different types of infection (skin, lung, CNS, etc) must all these indications be listed? It seems reasonable that a statement such as “this drug is used for a wide variety of bacterial infections” would suffice.

Even more problematic is the fact that some FDA-approved indications are rarely prescribed so that the inclusion of such indications may actually be confusing to a patient.

For example, some potassium iodide products are indicated as an expectorant, when such use is relatively rare.

### **Criterion 2**

*Line 199:* Inclusion of all contraindications (i.e., relative contraindications in particular) would be too proscriptive with respect to KG. From a clinical perspective, some contraindications are of questionable or little clinical significance. In a few cases, there are scientifically-valid criticisms of studies that engendered the contraindication (e.g., the study quoted for sulfonylurea hypoglycemic medications which supposedly demonstrated a link between cardiovascular disease and sulfonylureas). Also, there are situations where data has been extrapolated to other drugs inside or outside of the original drug's class. This extrapolation may or may not be of clinical significance and accuracy, according to authoritative secondary literature sources, or well-accepted national consensus guidelines such as the National Cholesterol Education Panel (NCEP). These authoritative sources are routinely utilized in the development of private CMI.

*Lines 207—208:* This recommendation is redundant – it is essentially the same as Lines 210—212. The intent of the term “information” is unclear, so provision of an example would be useful if this recommendation is not removed altogether.

### **Criterion 3**

*Lines 229—230:* While this is reasonable information to include, it is typically not part of the PI. Therefore, recommending routine inclusion amounts to holding private CMI to a higher standard than professional labeling.

*Lines 243—246:* The same significant error exists in this subsection as in the KG (see Components of Useful Information part G. Tolerance and Dependence).

The KG provides as follows: “‘Drug dependence’ may be defined as a pattern of behavior in which drug use is given a much higher priority than other behaviors that once had a higher value. It is not absolute, but exists in degrees, and its intensity is measured by the behaviors that are associated with the use of the drug.”

This is in fact a definition not of dependence but of addiction, which is essentially the exhibition of drug-seeking behavior. Addiction is relatively infrequent/rare, even with chronic narcotic use for approved indications such as cancer pain. In contrast, dependence is virtually universal in chronic narcotic use for approved indications, and is functionally defined as a physiological and/or psychological state such that abrupt drug discontinuation will elicit a predictable set of withdrawal symptoms.

Line 246 of the draft Guidance also incorrectly contains the term “addiction” instead of “dependence”, similar to the KG as noted above.

The relevance of this to CMI is very clear: addiction is relatively rare during supervised narcotic use. This is a crucial point to be included in CMI, since many patients (e.g., cancer sufferers) have an unfounded fear of “becoming addicted”, and instead of using their narcotic medication as directed, may needlessly suffer without chronic pain relief. Therefore, addiction potential should be addressed in private CMI, but with the incidence of occurrence addressed as well.

Conversely, it is important to correctly educate the patient regarding drug dependence, since this is relatively common with chronic narcotic use. Specifically, the consequences (specific withdrawal symptoms) of abrupt narcotic drug discontinuation (including the failure to properly refill ongoing prescriptions) need to be communicated, along with how to properly discontinue treatment (e.g., dose tapering) under medical supervision. This will encourage proper use and proper caution on the part of the patient.

*Lines 248—252:* The example of overdose reporting provided (“calling the doctor”) is inappropriate, since the standard advice for poisonings is to immediately proceed to a local emergency room, or call the national poison center hotline number for urgent assistance. Phoning a physician office would typically waste valuable time, even if the call was during office hours.

Symptoms of overdose should be included in CMI only when such symptoms are not confusing or misleading to a patient. For example, if an adverse effect of nausea is included in CMI, then if the overdose section also lists nausea as a symptom, some patients with uncomplicated, self-limited nausea may well be frightened unnecessarily, and inappropriately utilize emergency medical resources (Emergency Room or Poison Center). CMI should contain cardinal symptoms of overdose if they exist, and any overlap between adverse effects and overdose symptoms should only occur for very serious/life-threatening symptoms, such as ventricular arrhythmias.

#### **Criterion 4**

*Lines 263—265:* The draft Guidance is overly proscriptive with respect to the recommendation that all precautions should be included in CMI. The KG provides as follows: “If applicable, a statement or statements of precautions the consumer should take to ensure proper use of the medicine. (These statements are encouraged in serious situations.)”

#### **Criterion 5**

The KG state (Chapter 3 Components of Useful Information Part F) the following: Guidance for the definition of “adverse reactions” can be found in 21 CFR 201.57(g) as, “an undesirable effect, reasonably associated with the use of the drug, that may occur as part of the pharmacological action of the drug or may be unpredictable in its occurrence.” “Reasonably associated with use of the drug” is a reference to causality of adverse reactions—that is, did the drug possibly or probably cause the adverse reaction? Causality or lack thereof should therefore be considered, and guidance offered, since causality is an important clinical issue with respect to adverse reactions, as evidenced by the KG reference noted above.

*Lines 298—299:* This specific adverse reaction guidance is arbitrary and problematic. For example, what if there are less than five common adverse effects that are “reasonably associated with the use of the drug”?

#### **Criterion 8**

*Line 349:* Readability instruments (e.g., Fleish-Kincaid) may not accurately assess reading level for CMI. The use of generic drug names, longer sentences (e.g., lists of

adverse reaction symptoms or disease contraindications) in some CMI sections, and parenthetical explanatory professional terms where appropriate will misleadingly skew the results of readability instruments. That being said, we agree that the information in CMI should be expressed in language that is generally understandable at the middle school level.

**Conclusion:**

In conclusion, the draft FDA CMI Guidance document has been presented late in the overall chronology of CMI since the KG development in 1996, and FDA's draft guidance is of limited usefulness in the development and assessment of private sector CMI. CMI developers are dealing with thousands of private CMI documents in their respective databases. Therefore any potential changes driven by this draft guidance to those thousands of CMI documents may take months/years to complete. Further, as documented in part III above, the feedback loop between the agency and private sector and/or NCPIE has been problematic.

For the reasons stated herein, First DataBank respectfully requests FDA to adopt the following:

Assuming that significant progress is demonstrated by the private sector as derived from the FDA's planned 2006 assessment of CMI pursuant to P.L. 104-180, apply the results of the 2006 CMI assessment towards the mid-course evaluation of Healthy People 2010 key objectives (below) and subsequently link/conduct the final assessment of CMI in 2010 in conjunction with the final assessment of Healthy People 2010 Medical Product Safety Objectives 17-4 and 17-5 (for which FDA has lead federal agency status). These two objectives align directly with the provision of useful information to consumers. They are:

- 17-4. Increase the proportion of patients receiving information that meets guidelines for usefulness when their new prescriptions are dispensed ("guidelines" refers to the Action Plan for the Provision of Useful Prescription Medicine Information);
- 17-5. Increase the proportion of patients who receive verbal counseling from prescribers and pharmacists on the appropriate use and potential risks of medications (via FDA's existing, ongoing consumer telephone survey).

First DataBank stands ready to work constructively with FDA in the private sector CMI arena. We look forward to moving the private sector CMI process forward in cooperation with FDA and NCPIE.

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