Questions and Answers About the New Content and Format Requirements for Prescribing Information

Q: Why is FDA changing the content and format of prescribing information for drugs?

A: These changes are part of a larger FDA initiative to manage the risks of medical product use and reduce medical errors by healthcare professionals, as well as enable them to better communicate risk information to their patients. Developments in recent years have contributed to an increase in the length, detail and complexity of prescribing information for drugs. The revisions will make it easier for healthcare professionals to access, read and use prescribing information, thereby increasing the extent to which they rely on it to obtain information on prescribing, dispensing and administering prescription drugs. These revisions should enhance the safe and effective use of prescription drug products and in turn reduce the number of adverse reactions resulting from medication errors due to misunderstood or incorrectly applied drug information.

Q: What is the "prescribing information" for drugs that will have to be revised?

A: Prescribing information is also known as "labeling," "package insert," "professional labeling," "direction circular," or "package circular." The revised content and format requirements apply only to the prescribing information of FDA-approved prescription drug and biological products. The requirements do not apply to over-the-counter drug products. The requirements also do not change the content or format of FDA-approved patient information, including Medication Guides.

Q: What are some of the key changes required by the final rule and how will prescribing information change?

A: The most notable difference will be that new and recently approved products' prescribing information will include *Highlights* of prescribing information and a *Table of Contents*. *Highlights*, which typically will be 1/2 page in length, will provide immediate access to the information that healthcare professionals most commonly refer to and view as most important. The other requirements include reordering certain sections, minor content changes and minimum graphical requirements for the format.

Q: Other than summarized information, what additional innovations does *Highlights* offer health care professionals?

A: For quick and easy reference, *Highlights* will include:

- Date of approval of the original drug product.
- The *Recent Major Changes* section will list all substantive changes made within the past year to the following sections of the prescribing information: *Boxed Warning*, *Indications* and *Usage, Dosage and Administration*, *Contraindications*, and *Warnings and*

Precautions. These changes will be identified within the full prescribing information as well.

- Adverse drug reaction reporting contact information.

Q: What are the most significant changes to the format and ordering of the prescribing information?

A: The most significant format and section reordering changes include:

- The information practitioners refer to most frequently and consider most important (e.g. *Boxed Warning*, *Indications* and *Usage, Dosage and Administration*, and Dosage Forms and Strengths, separated from Storage and Handling) will be located at the front of the prescribing information.

- Risk information will be consolidated. The *Adverse Reactions* section will follow after the *Warnings and Precautions* section, consolidating risk information in one location and helping to put in context the relative seriousness of the adverse reactions discussed.

- Other information formerly found in the *Precautions* section will be located in sections devoted to *Use in Specific Populations*, *Drug Interactions* and *Patient Counseling Information*.

- A separate *Patient Counseling Information* section will be added to the new requirement that all FDA-approved patient information be reprinted in or accompany the drug product's prescribing information. The purpose of this change is to increase the prominence of patient information. The requirement regarding the inclusion of all FDA-approved patient information applies also to older products not otherwise subject to the new content and format requirements.

- There will be standardized bolding, white space and established minimum font sizes to enhance communication of important information.

Q: Why require a *Boxed Warning* in *Highlights*, when a *Boxed Warning* is also at the top of the Full Prescribing Information (FPI)?

A: As with all information in *Highlights*, the *Boxed Warning* in *Highlights* is a summary, not a duplication of the full *Boxed Warning* in the FPI. It typically will be in a bulleted format, limited to 20 lines and will refer to more detailed information, including the complete *Boxed Warning* and other sections of the FPI. Because *Highlights* is 1/2 page in length and the *Table of Contents* follows, *Highlights*' *Boxed Warning* will rarely, if ever, appear on the same page of the prescribing information as the full *Boxed Warning*. FDA believes a summarized *Boxed Warning* in *Highlights*, with references to more detailed information, is the most effective way to communicate critical safety information to healthcare professionals.

Q: Why is FDA requiring both *Highlights* and *Contents*?

A: *Highlights* and *Contents* serve different purposes. *Highlights* presents a succinct summary of the information that is most crucial for a drug's safe and effective use, with cross-references to more details in the full prescribing information. It includes information from only certain sections of the full prescribing information. In contrast, *Contents* serves as a navigational tool that references all the sections and subsections in the full prescribing information, some of which will not be referenced in *Highlights*.

Q: How will the content and format revisions to the prescribing information work in conjunction with FDA's electronic initiatives?

A: On November 2, 2005, the FDA began requiring drug manufacturers to submit prescription drug labeling information to FDA in a new electronic format. Using embedded computer tags and standardized medical terminology, the new format will enable physicians to quickly search and access specific prescribing information and thereby help reduce medication errors. The new electronic product labels will be the key element and primary sources of medication information for "DailyMed", a new interagency online health information clearinghouse created cooperatively by the FDA and the National Library of Medicine (NLM) for the benefit of patients and healthcare professionals. "DailyMed" can be accessed for free at http://DailyMed.nlm.nih.gov.

In the future, this new information will also be provided through the facts@fda website, a comprehensive Internet resource designed to give one-stop access to information about all FDA-regulated products.

Q: Who will be affected, how, and how have affected parties provided input?

A: The primary users of prescribing information, healthcare professionals, will benefit most by these revisions. FDA evaluated the usefulness of prescribing information among healthcare professionals to determine whether and how its content and format could be improved. It used surveys, developed prototypes, conducted focus groups, and held a public meeting to solicit comments prior to issuing a proposed rule for general public comment. It received and carefully considered 97 comment submissions from pharmaceutical and trade representatives, professional organizations representing healthcare professionals, consumer advocacy organizations, individual physicians, pharmacists, and other affected parties when developing the final rule.

Comments expressed broad agreement that prescribing information could be more effective in communicating drug information and overwhelming support for FDA's goal of improving the content and format and for the proposed reordering of sections. Manufacturers, the primary authors of prescribing information, expressed concerns about elements of the proposed rule, including the requirement for *Highlights*. FDA fully addressed these comments in the preamble to the final rule.

Q: How did FDA change the proposed rule to address comments?

A: In response to comments and on its own initiative, FDA made a number of substantive changes to the proposed rule, some of which include:

- Made improvements to *Highlights*, such as: the summarized *Boxed Warning* and the addition of a heading to describe recent major changes.

- Consolidated safety information and retained the current definition of adverse reactions, with clarifying language.

- Reorganized to improve access to commonly referenced prescribing information about dosage forms and strengths. This information will be presented in a section separate from storage and handling information.

Q: Will all prescribing information for human drug and biological products be required to conform with the new content and format requirements?

A: No. The new requirements only apply to new and recently approved prescription drugs. This includes those that were approved on or after the effective date of the final rule, drugs that have been approved in the five years prior to the effective date of the final rule, and older drugs for which there is a major change in the prescribing information (e.g., approval of a new use). Many older approved drug products are not required to meet the content and format revisions, though they may have to provide additional patient information. They can voluntarily revise their prescribing information.

Q: Why did FDA conclude that it was in the public interest to exempt some drugs from the requirements of the final rule?

A: FDA believes that applying the revised content and format requirements only to recently approved products is the most reasonable approach to maximizing the public health benefit using available resources. FDA carefully considered the costs and benefits of implementing the revised format and determined that it would be an excessive burden to require revisions to the prescribing information of all prescription drugs. Healthcare professionals are more likely to refer to the prescribing information of recently approved products. Also, the prescribing information for newer products is typically longer and more complex, and thus more likely to benefit from a new format that makes information more accessible. FDA intends to engage in a comprehensive educational campaign to educate healthcare professionals about the major features of the new format.

Q: Will FDA provide any exceptions (i.e., small business, hardship cases) to those parties subject to the rule?

A: The compliance requirements for small entities under the final rule are the same as those described above for other affected entities. FDA received no comments from small entities or from entities claiming the requirements would impose a hardship upon them. Compliance

primarily involves designing prescribing information that conforms to the content and format requirements. Because manufacturers already submit prescribing information with New Drug Applications (NDA), Biologics License Applications (BLA) and efficacy supplements to FDA, no additional skill will be required to comply.

Q: When will the rule go into effect or when will prescribing information have to comply with new requirements?

A: There is a staged implementation schedule designed to most effectively use FDA's resources to approve new supplements. The rule goes into effect on June 30, 2006. New applications will be required to conform with the new content and format requirements as soon as the rule goes into effect. Drug products approved within the past five years will gradually be required to contain revised prescribing information, based on how recently the drugs were approved. Drugs approved within the year prior to the rule have three years before being required to contain updated prescribing information. Drugs approved between years one and two prior to the rule have four years to be updated with revised prescribing information, and so on, until those that were approved between years four and five have been updated with the revised prescribing information within seven years. Drug manufacturers with drugs approved five years or more before the rule's effective date can voluntarily revise prescribing information at any time. All FDA-approved patient information will have to be reprinted in or accompany drug products' prescribing information within one year of the rule's effective date.

Q: What are the costs and benefits of the final rule?

A: FDA estimates the quantifiable benefits of the final rule over 10 years to range from $330 million to $380 million and from $420 million to $480 million at a 7 and 3 percent discount rate, respectively. Direct costs of the final rule are projected to range from approximately $7 million to $17 million in any one year, for a total present value of approximately $90 million and $120 million over 10 years at a 7 and 3 percent discount rate, respectively. The FDA has concluded that the benefits of the final rule outweigh the costs. Benefits include better informed prescribers, improved risk management, improved communications with patients, and a mechanism to facilitate electronic initiatives.

Q: Why does FDA require FDA-approved patient information to be reprinted in, or accompany, prescribing information when it also requires patient information in the *Patient Counseling Information* section?

A: FDA-approved patient information and the information in the *Patient Counseling Information* section have distinct purposes. *Patient Counseling Information* is specifically written for healthcare professionals to inform them about what information is important to convey to the patient at the time of prescribing for the drug to be used safely and effectively. FDA-approved patient information, in contrast, is specifically written for a lay audience and is intended to be read by patients. FDA believes that both of these are important tools to provide information for patients making it more beneficial and effective.

Q: The proposed rule would have revised the requirements for the content of prescription drug product container labels. What happened to these revisions?

A: FDA withdrew the proposed revisions for the content of prescription drug product container labels because it intends to conduct a comprehensive evaluation of information required to be contained on product labels. If necessary, FDA will propose changes to these requirements after that evaluation has been completed.

Q: How does FDA plan to help facilitate the implementation of the content and format requirements?

A: In coordination with the publication of the final rule, FDA also published four guidance documents.

- Labeling for Human Prescription Drug and Biological Products - Implementing the New Content and Format Requirements. This draft guidance focuses on, among other things, how to determine what information should be presented in *Highlights*.

- Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products - Content and Format. This final guidance focuses primarily on how to organize the large body of complex information that is typically contained in the *Adverse Reactions* section and discusses how to determine whether a reported adverse event should be included in the *Adverse Reactions* section.

- Clinical Studies Section of Labeling for Human Prescription Drug and Biological Products - Content and Format. This final guidance focuses on how to select the studies that are appropriate for inclusion in the *Clinical Studies* section and what information should be provided for those studies.

- Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drug and Biological Products - Content and Format. This draft guidance focuses on how to determine whether an adverse reaction should be discussed in the *Warnings and Precautions, Contraindications*, or *Boxed Warning* sections and what information should be provided for the adverse reaction.

FDA also has developed several prototypes (or examples) of prescribing information that illustrate approaches to complying with the content and format requirements. These and other educational materials will be posted in a dedicated area of the FDA website. Furthermore, FDA plans to engage in external outreach and training for industry, healthcare professionals and interested consumers, in addition to internal training programs for FDA reviewers.