



August 26, 2008

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

**Re: Docket No. FDA-2006-N-0515, RIN 0910-AF11, Content and Format Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling, Proposed Rule**

Dear Sir/Madam:

The American Society of Health-System Pharmacists (ASHP) is pleased to submit written comments pertaining to the proposed rule related to content and format labeling for human prescription drug and biological products; Requirements for pregnancy and lactation labeling (proposed rule). For more than 60 years, ASHP has helped pharmacists who practice in hospitals and health systems improve medication use and enhance patient safety. The Society's 35,000 members include pharmacists and pharmacy technicians who practice in inpatient, outpatient, home-care, and long-term-care settings, as well as pharmacy students.

ASHP is pleased that the Food and Drug Administration (FDA) has published this proposed rule. The Society is also pleased that the agency is looking at ways to improve labeling to provide more complete information about the effects of medicines used during pregnancy and breastfeeding. However, ASHP is concerned that these proposed changes to the content and format requirements for prescription drug labeling, specifically FDA's proposal to entirely eliminate the current pregnancy categories A, B, C, D, and X, fails to create a consistent and useful format for decision-making, and may ultimately have a negative impact on medical decision making on drug use during pregnancy.

Elimination of Pregnancy Categories

Major initiatives in medical informatics have been and are being launched, including initiatives developed and financed by the federal government, resulting in a growing recognition of the importance of codifying and adequately summarizing a wide variety of

health information to support clinical decisions. There is also a growing recognition that clinicians must address an exponential growth in information, and navigate through the most clinically relevant data for individual patients.

ASHP is strongly concerned that FDA's proposed labeling requirements could result in potentially lengthy prose discussions of risk without an associated schema to support algorithmically driven logic. ASHP is further concerned that, without an associated schema, there will be no consistent and useful format for decision-making. Given a lack of standardization of labeling requirements by the FDA, the private sector may develop a wide array of schema and associated rules to support pregnancy risk decisions about drugs. Thus, a clinician may receive different advice about the same drug depending on which decision-support knowledgebase is employed. Additionally, reliance on narrative discussions alone to drive risk assessment decisions may have an unintended consequence of compromising patient safety due to difficulty in interpretation and the growing amount of competing risk information in labeling.

ASHP strongly recommends that FDA engage the necessary expertise, both internal and external, to develop and test a clinically relevant standardized schema to represent the risk continuum in pregnancy and lactation labeling. FDA should require that pregnancy and lactation labeling include the information contained in the proposed rule, in addition to a rating system.

#### Focus Group Testing

FDA relied on focus group testing to develop the proposed labeling. For example, in May 2000, FDA conducted four focus groups to evaluate standard statements being considered by the agency to use in pregnancy labeling to characterize the risk of developmental abnormality associated with a drug. However, none of the focus groups used by FDA to develop the proposed labeling appear to have included pharmacists. Since interpretation of the new format will likely fall predominantly to pharmacists, ASHP recommends that FDA perform focus group testing that includes pharmacists prior to implementing any new regulations relating to pregnancy and lactation labeling.

#### Ordering of Pregnancy Labeling Components

ASHP is pleased that the proposed "Pregnancy" subsection would require prescription drug labeling to contain the following information: (1) Pregnancy exposure registry information (if applicable), (2) a general statement about the background risk of fetal developmental abnormalities, (3) a fetal risk summary, (4) clinical considerations, and (5) data.

In order to optimize the clinical usefulness of this labeling subsection, the Society recommends that the risk information should appear first, since this labeling is used mostly by health care professionals in making prescribing decisions, followed by the

pregnancy registry contact information. ASHP recommends the following order: fetal risk summary, information on background risk, and pregnancy registry contact information. The Society recommends that patient education materials display the pregnancy registry contact information more prominently, possibly listing it first.

#### Implementation Plan

ASHP is concerned that holders of applications approved prior to June 29, 2001 are not required to implement the new content requirements under the proposed rule. Instead, if the labeling for such applications contains a pregnancy category, the application holders will be required to remove the pregnancy category designation by 3 years after the effective date of the pregnancy final rule. A significant number of drugs will therefore have labeling that is inconsistent with preferred practice. ASHP recommends that FDA require holders of applications approved prior to June 29, 2001 to include a pregnancy section in their labeling that includes at least some of the requirements that will be included in the final rule.

ASHP appreciates this opportunity to present its written comments pertaining to the proposed rule. 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](mailto:jcoffey@ashp.org).

Sincerely,

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

Justine Coffey, JD, LLM  
Director, Federal Regulatory Affairs