DAIICHI

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June 21, 2001

Docket No. 00N-1269

Dockets Management Branch (HFD-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20857

Dear Sir/Madam:

Please find comments to Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Products; Proposed Rule, December 22, 2000.

Daiichi Pharmaceutical Corporation has reviewed the Proposed Rule and finds that many of the proposed changes could make the label a more effective instrument for providing healthcare professionals easier access to the important efficacy and safety information presented in the label. We do have the following comments about specific parts of this proposal:

1. The Agency in its joint FDA-Drug Information Association "CDER Live" presentation on the Proposed Rule noted that only 5% of physicians obtain label information from the Package Insert (PI). To improve accessibility, the Agency has ongoing initiatives that will make the label available electronically. Because of this, rather than specify a great deal of detail on the required format of the PI, the Agency should allow flexibility as to font size, organization of columns and size of paper. For example, columns are often difficult to read on a video monitor, and legible font size may be different for an internet-based PI versus a paper-based PI. Flexibility in such requirements would allow the presentation of information to be optimized for the specific media in which the PI is being presented.

   Additionally, the Agency may need to further consider the impact of the proposed requirements on paper size, particularly in light of the cost of paper and the mechanisms by which various configurations of paper can be attached or stuffed into the product.

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2. The Highlights Section must be large enough to properly convey the appropriate risk information. The space allocation for the Highlights Section should not be unduly limited. Each drug is different and must be evaluated in light of its own risk-benefit profile. For some drugs, the "important" information may be fairly easy to encapsulate. For other drugs, it may be nearly impossible. There are products, for example, that have several indications within one PI and the Agency should not restrict the summary information that is necessary to be communicated by arbitrarily restricting the space required to convey this important information.

   Furthermore, the information most important to one healthcare provider for one diagnosis may not be what is important to another healthcare provider for another diagnosis. Although the Highlights Section would attempt to identify the most important information, what is most important will vary based on the particular healthcare provider viewing the label.

3. In general, the Proposed Rule attempts to provide healthcare practitioners with a prominent summary of the minimum required information that they need to know to safely and effectively administer the drug, and a fuller presentation of relevant safety and efficacy data available at a later point in the PI. The dichotomy between these two presentations can be substantial depending upon the indications for which a drug has been approved. Consider the multiple approved indications for an antibiotic like moxifloxacin. It would require a considerable amount of text to summarize all of the safety and efficacy data related to each indication. Efficacy data to support indications would clearly require separate treatment for each indication, although it would be helpful to present safety data according to: routes of administration, total daily dosages, duration of therapy, and other factors that may relate to administering the drug in different populations and/or patients with different diseases.

   The use of an inverted triangle (▼) to communicate the length of time that the product has been on the market is problematic. Labels may be in distribution longer than the designated time period. For instance, if a product has a three year expiration date and it is made and packaged at the end of the proposed 3 year use of the ▼, this PI could be in commerce for twice as long as the time suggested in the Proposed Rule. In addition, a label may change for many reasons, such as the addition of new indications. Is there a need to inform practitioners of these new changes to the label? Reconsideration of how this section of the Proposed Rule will be implemented to convey clear and useful risk assessment information to healthcare providers may needed.

4. The exclusion of *in vitro* data is also problematic. As an example, in the anti-infective class of agents, this information is often used as a last resort by healthcare providers for treating critically ill patients. Without such information, they have no guidance. There are also healthcare providers in isolated rural areas whose small hospital or reference lab cannot provide a meaningful antibiogram in the required

timeframe. Information in the PI on *in vitro* microorganism susceptibility from large scale clinical trials or surveillance data would provide healthcare providers with information to address common as well as "worst case" scenarios and allow some basis for making an informed decision regarding the possible efficacy of an anti-infective agent for a pathogen while awaiting susceptibility testing.

In other therapeutic classes, *in vitro* activities as well as data from animal studies provide valuable information for healthcare providers in understanding the risks associated with the use of a specific product.

The revision of the content and format of the label in order to convey the risk/benefit information to healthcare providers in a clear and concise manner is important. We believe that our comments on the Proposed Rule will significantly contribute to this goal.

Sincerely,

Amy S. Domanowski

Amy S. Domanowski, Ph.D.

Executive Director
Regulatory Affairs

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