



April 25, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Risk Management — Risk Management Programs – FDA Docket No. 02N-0528

Dear Dockets Management Branch:

I am writing on behalf of the Pharmaceutical Printed Literature Association (PPLA) regarding the request for comments on Risk Management Programs (RMPs) published by the U.S. Food and Drug Administration as FDA Docket Number 02N-0528 in the March 7, 2003, *Federal Register* (Volume 68, Number 45). The PPLA strongly endorses FDA's initiation of a program approach to minimizing risks throughout a drug product's lifecycle to optimize its benefit/risk balance. The PPLA further welcomes the opportunity to comment on FDA recommendations presented in the Concept Paper entitled *Risk Management Programs*, released by the Agency on March 3, 2003.

As outlined in these comments, however, the PPLA maintains that enhancements should be made such that the forthcoming guidance:

- Harmonizes with European practices that incorporate patient information aggressively and ubiquitously into prescription drug distribution and marketing;
- Calls for broader use of patient package information (PPI) with prescription drug products; and
- Maximizes consistency in drug product information by establishing FDA-approved language for use in PPIs and Medication Guides.

PPLA Background

The PPLA is a not-for-profit association chartered in 2001 to serve as the voice of pharmaceutical printed package information manufacturers, and provide a forum for members to promote and improve delivery of information for protection of patients. To do so, the PPLA works to support health care professionals, and advocates use of printed literature to legislative, regulatory and other decision-making bodies. Additionally, PPLA acts as an educational resource for strategic partners and the public.

As a young association, PPLA's core initial goal is to help the pharmaceutical industry help consumers benefit from existing and new drugs - a return on investment of billions of research and development dollars - by taking those drugs as prescribed, with instructions, precautions and risk data clearly understood. The desired outcome is a win-win-win situation: consumers enjoy better health, the healthcare system operates at lower total cost, and drug manufacturers report higher sales.

PPLA Comments

The PPLA respectfully submits the following labeling-specific recommendations with regard to the Risk Management Programs concept paper.

Section IV, Parts B, C and D:

1. The PPLA disputes the position that PPIs should be limited to RMP Levels 2 and higher. Existing models and practices in the European Union (EU) that are also endorsed by the World Health Organization (WHO) come down strongly on the side of expanded patient information as a critical risk management tool. In addition, organizations such as the New Zealand Ministry of Health, and the European Agency for the Evaluation of Medicinal Products advocate information levels beyond those currently advanced in the United States.

In the US, pharmaceutical product information exists for physicians and pharmacies, but not in any consistent, comprehensive or comprehensible form for the patient. In Europe, however, the patient is included as a critical audience relative to approval and marketing of prescription drugs. Moreover, WHO specifies that patient information must be compliant with standards set by the appropriate drug regulatory authority (DRA) – these are European equivalents of the U.S. Food and Drug Administration.

As explained by the WHO in its *Essential Drugs and Medicines Policy*, Annex 8 (paragraph 29):

Adequate information on the use of medicinal drugs should be made available to patients...When package inserts or leaflets are required by governments, manufacturers or distributors should ensure that they reflect only the information that has been approved by the country's drug regulatory authority. If package inserts or leaflets are used for promotional purposes, they should comply with the ethical criteria enunciated in this document. The wording of the package inserts or leaflets, if prepared specifically for patients, should be in lay language on condition that the medical and scientific content is properly reflected.

During FDA's Risk Management Workshop that was held on April 10, 2003 in Washington, DC, FDA officials maintained that the U.S. is at the forefront of risk management, relative to other countries, with regard to looking at risk in a comprehensive way. This statement seems to be refuted by policies and practices considered to be fundamental good management and marketing practice throughout other parts of the world (especially Europe) where the patient is entitled to the same quality of drug information as are medical practitioners. This disparity should be addressed by harmonizing FDA guidelines with those in place in the EU.

The PPLA believes that FDA has an historic opportunity to more effectively involve patients in the risk management process by following EU practices whereby PPIs – along with package inserts (PIs) intended for use by physicians and pharmacy personnel – play a major role in optimized use of pharmaceutical products.

FDA should strongly consider requiring that PPIs be distributed with more drug products. To that end, the PPLA specifically recommends that PPIs be required labeling for all newly-approved drug products as a beginning; at some point in the future PPI labeling requirements should be phased in for products that are already on the market.

2. FDA has asked for comment on how RMP tools can be best selected or developed. The PPLA urges adoption of the PPI as an essential tool, both for maximum risk reduction and optimum realization of medication benefit.

as an RMP candidate. Such an approach would also halt the product-by-product approach to risk management that, as noted during the April 10 conference, places the information burden on the pharmacist.

Pharmacy representatives who commented during the April 10 meeting further voiced concern over the possibility of liability due to inconsistent and incomplete sponsor-provided, FDA-approved, patient information. A requirement for FDA-approved, manufacturer-provided PPIs should afford an additional degree of liability protection, as well as improved patient protection. Additionally, drug product information would be made consistent in this way – an outcome endorsed by the Pharmaceutical Research and Manufacturers Association (PhRMA). The PPLA joins with PhRMA in the view that no Rx product is risk free; patient information is the key to measurably reducing the degree of risk via uniform and approved information.

PPLA further wishes to put on record our strong disagreement that the PI – along with post-approval surveillance – constitutes an appropriate level of effective risk management. The PPLA joins with the numerous representatives of trade and patient safety advocacy in force April 10 who noted that the cornerstone to optimized risk management is an information triad consisting of the PI, PPI and post-approval surveillance.

In answer to a question the PPLA posed to FDA during the April 10 workshop, the Agency conceded that PPI-appropriate language already is included with many new drug applications. The addition of this language, the Agency observed, is becoming more common as manufacturers increasingly engage in direct-to-consumer advertising. The PPLA asks FDA to leverage and expand current practice to formalize safety information for consumers, as well as for physicians and pharmacists.

3. As a final comment, the PPLA acknowledges certain benefits of electronic labeling systems envisioned by PhRMA, but we take issue with whether these types of systems should be viewed as a substitute for printed PI's. Indeed, instead of being referred to as a "paperless labeling" initiative, we believe these systems should be viewed as an "electronic update" initiative. That is, no matter how popular these envisioned systems ultimately prove to be, it would be a tremendous mistake to use them as a substitute for printed PI's.

Considering the myriad possibilities for telecommunications failure, power outages, computer hacking, terrorism, and other threats to all sorts of electronic systems, the PPLA asserts that electronic labeling systems can only work successfully as an adjunct to, *not a replacement for*, printed PIs. Moreover, since FDA has no authority over the dispensing of drug products, the Agency would have no ability to ensure that electronic systems are being used correctly, or are being used at all, by every dispensing site in the country. It would, therefore, be a significant setback for public safety if the Agency elected to eliminate regulatory requirements that a printed PI accompany every container of drug product shipped by the manufacturer.

Conclusion

The PPLA thanks FDA for this opportunity to comment on the Agency's risk management initiatives, and strongly supports the Agency's efforts to seek new ways of maximizing patient benefit while minimizing risk. We do, however, urge the Agency to include patients in this effort instead of relying solely on PIs and post-marketing surveillance. Lastly, the PPLA wishes to offer its full resources to assist FDA as the Agency develops and implements its risk management programs.

Sincerely,

Peter G. Mayberry
Executive Director