PHARMACEUTICAL PRINTED LITERATURE ASSOCIATION

252 NORTH WASHINGTON STREET • FALLS CHURCH, VIRGINIA 22046
PHONE: 703-538-5799 • FAX: 703-538-6305 • WWW.PPLAONLINE.ORG

August 28, 2003

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

RE: Comments -- Current Status of Useful Written Prescription Drug Information for Consumers: Public Meeting - FDA Docket No. 03N-0168

Dear Dockets Manager:

I am writing on behalf of the Pharmaceutical Printed Literature Association (PPLA) to comment on issues raised during the public meeting on the Current Status of Useful Written Prescription Drug Information for Consumers that was convened by the U.S. Food and Drug Administration (FDA) in Washington, D.C. on July 31, 2003 (Docket No. 03N-0168).

During the public meeting, the PPLA was encouraged by the numerous views expressed in support of the need for manufacturer-provided, FDA-approved written literature dispensed with all prescription drug products.

While the PPLA has no formal affiliation with consumer health advocacy organizations such as the Center for Medical Consumers, Public Citizen, and the National Women's Health Network, we share their view that the voluntary system has been a failure (i.e., the information being provided is not useful in about 50 percent of all cases, and the goal of 95 percent distribution has not been met), and fundamental changes to the distribution system of useful patient information are very much in order.

Basis for Comments: PPLA Background

The PPLA is a not-for-profit trade association established in 2001 to serve as the voice of the pharmaceutical printing industry. PPLA members include printers of pharmaceutical inserts, labels and cartons, as well as suppliers to the pharmaceutical printing industry and machinery manufacturers.

PPLA members represent the majority of the North American pharmaceutical printed-insert industry, and the association strives to provide a forum for worldwide members to advance patient safety and risk communication. The PPLA supports health care professionals, and advocates use of printed literature to

legislative, regulatory and other decision-making bodies. In addition, PPLA is 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 helping patients take 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. For more information about the PPLA, I invite you to visit our website at www.pplaonline.org.

Comments

As we approach 2006, the PPLA reiterates our opinion – and echoes the opinions of other groups who spoke during the July 31 meeting – that FDA should change course now, and begin implementing requirements that manufacturer-produced, FDA-approved, printed patient information be dispensed with all prescription drug products at the earliest possible date.

While the PPLA takes no position with regard to program implementation phases, or implementation sequencing by drug name or type, we do note that it has been 28 years since FDA first attempted to require useful drug information for patients, and further delays will serve no useful purpose. We also note the wealth of scientific data regarding the effectiveness and need for useful printed literature, and contend that legal authority enabling FDA to take action exists under PL 104-180.

Indeed, a significant change in direction is warranted under PL 104-180 because research shows that the goal of having 95 percent of all prescription drugs dispensed with useful patient information by the year 2006 is not being met, and mere tweaking of the current system will not be sufficient to meet this goal. As detailed at the July 31 hearing, research shows that the information currently being dispensed to patients is not useful in some 50 percent of those instances where any information was provided at all, and some one-in-ten pharmacies dispensed no information at all.

We further note that our recommendations are economically and technical feasible, especially given that: 1) manufacturer-produced, FDA-approved patient package inserts (PPIs) have already been developed for many of the most frequently prescribed drugs, and 2) package inserts (PIs), that can be used as the basis for PPIs, already exist for all FDA-approved drug products. In addition, as we demonstrated at the July 31 public meeting, the means to distribute sufficient quantities of PPIs attached directly to pharmaceutical packaging is already in place. This packaging capability alleviates the need for pharmacies to house leaflets separately on their premises.

By requiring that manufacturers attach removable leaflets as part of their approved labeling, therefore, the PPLA contends that: 1) consumers will benefit from having universal availability to useful printed literature; 2) dispensing sites will not be burdened with filing cabinets full of leaflets; 3) dispensing sites will not have to undergo significant alteration to their workflow practices; and 4) FDA will meet its goal for availability of useful drug information being dispensed to patients.

While the PPLA contends that the gold standard of pharmaceutical distribution would be unit-of-use packaging by the manufacturer with a PPI included in each package, we recognize that the current paradigm

of bulk distribution has become entrenched in the United States. This is unfortunate for numerous reasons – one of the primary ones being that bulk distribution inherently requires pharmacy re-packaging of drug products which, in turn, often results in dispensing errors, loss of efficacy, counterfeiting opportunities, product tampering, diversion, and other negative outcomes.

It is also unfortunate because bulk distribution of drugs in the United States is somewhat unique among industrialized countries worldwide. Despite the fact that many countries in the European Union, Asia and the Americas have adopted unit-of-use distribution for pharmaceuticals – and U.S. pharmaceutical manufacturers seem to have no problem packaging in those formats for those markets – the United States clings to an inferior distribution system that offers only one primary benefit: it is less expensive for drug manufacturers.

We urge FDA, therefore, to use this unique opportunity to begin converting the existing paradigm by requiring that drug products in the United States be dispensed at the earliest possible date in unit-of-use packaging with a manufacturer-produced, FDA-approved leaflet.

If this recommendation is deemed not feasible by the Agency at this time, however, the PPLA urges the Agency, at the very least, to require that a sufficient quantity of manufacturer-produced, FDA-approved PPIs is attached to each bulk container of drug product to ensure that sufficient quantities are available for distribution to the patient for each prescription presented.

Issues Raised During FDA's July 31, 2003, Public Meeting

With the remainder of our comments, the PPLA will specifically address a number of issued raised during the July 31 public meeting.

1. ***Patient leaflets typically are the product of "single-pass" printing systems used by the majority of pharmacies, affording economic convenience for pharmacies, and are supported by pharmacy associations as well as the National Council on Patient Information and Education (NCPIE). These organizations maintain that single-pass systems can work with FDA assistance.***

   Single-pass distribution (i.e., one sheet of paper passes through a pharmacy's printer one time for a prescription) of patient information at the pharmacy is inherently inferior. As acknowledged by Dr. John Coster of the National Association of Chain Drug Stores at the July 31 meeting, pharmacists depend on a network of some 80 companies – none of which are subject to any sort of regulatory oversight – to provide the information contained in patient leaflets.

   Dr. Coster further acknowledged that pharmacists "don't know where" the information comes from that these database and software vendors use for the leaflets. As a result, patients have no assurance that the information is accurate, complete or consistent from one pharmacy to another.

   In addition, single-pass systems: 1) inherently limit the amount of information that is made available to the patient; 2) typically cannot print graphics; 3) typically cannot print in color; and 4) are subject to mechanical failure in the pharmacy.

2. ***Pharmacies currently have the ability to alter patient information provided by vendors, which is laudable because this ability improves patient communication and pharmacy efficiency.***

The PPLA maintains that the ability to alter patient leaflets, and the practice of doing so, is contrary to the best interests of patients. As noted by Dr. Coster, pharmacists sometimes "edit" prescription information so it will not "scare" patients (Dr. Coster's words in quotes). This situation is made considerably worse by the fact, as cited at the July 31 meeting, that a majority of pharmacists provide no counseling to patients.

A great many learned healthcare experts strongly oppose such practices whereby critical information regarding a drug's potential side effects or indications is arbitrarily withheld. Indeed, as Dr. Janet Woodcock, M.D., Director of FDA's Center for Drug Evaluation and Research, observed in a 2000 public workshop while discussing the importance of written information in FDA's effort to move the risk management system for drugs forward, "A century or more of a professional model that didn't trust patients with information has created much inertia to be overcome."[1]

The potential for negative repercussions from pharmacy alteration of information was also noted in a 2002 *Washington Post* article[2] that described how at least one major chain pharmacy in the Washington, D.C. area was found to have violated provisions of its vendor contract prohibiting the alteration of leaflet text by removing sections entitled "Before using this medication," "Overdose," and "Additional information." The pharmacy's reason for routinely altering this information was that its single-pass printing system cannot accommodate more information than that which fits on one page of paper.

In fact, it is well documented that paragraphs or sentences may be removed at the pharmacist's discretion, even at the risk of legal action by the vendor, and potential health risks to patients. The PPLA can provide more detailed anecdotal information if useful to FDA.

3. ***Private industry is on track to meet the Year 2006 goals as evidenced by the high ratings achieved in making written information available; the information can relatively easily qualify as useful with educational and content-specific guidance from FDA.***

The PPLA disagrees with this assertion on three fronts:

- According to Dr. Bonnie Svarstad's data in the University of Wisconsin study, "Evaluation of Written Prescription Information Provided in Community Pharmacies," one in ten pharmacies researched did not provide *any* information to patients filling prescriptions. Dr. Svarstad suggested at the July 31 meeting that many pharmacists simply choose not to provide available information. FDA has no authority to require these pharmacies to implement the steps needed to provide such information, and these data suggest that the goal of 95 percent of all prescriptions be dispensed with useful written information by 2006 simply cannot be met. Moreover, there are no guarantees that the existing systems will always be operable as machines are prone to breakdown.

- As noted on July 31 by Dr. Alan Goldhammer of the Pharmaceutical Research and Manufacturers Association (PhRMA) – and reinforced by other participant comments – if patient information is not

---

[1] "Current Status of Useful Written Prescription Drug Information for Patients: Summary of Public Workshop," FDA, Feb. 29-March 1, 2000.

[2] "Not-So-Fine Print; Patient Drug Leaflets Omit Key Warnings, Other Information," Francesca Lunzer Kritz, *Washington Post*, HEALTH section, p. F01, August 13, 2002.

physically attached to prescription packages, many patients will be unable to receive any information. He and others cited situations in which the patient has no access to a learned intermediary such as when prescriptions are filled via the telephone, mail order, or drive-through pharmacy. Other situations mentioned included field-based dispensing physicians and mobile pharmacies that are common in many rural areas of the United States.

- The PPLA further observes for the record the well-established fact that, while information is generally made available, it is of poor quality as noted by FDA and the Agency's research resources.

- Of particularly poor quality, according to Dr. Svarstad, are the so-called abbreviated leaflets that a great many pharmacies distribute to patients.

4. ***Private industry cannot support the costs and production logistics that FDA-approved, manufacturer-produced printed patient information would entail if made mandatory for every prescription drug product.***

   The PPLA counters these claims as follows:

   - All pharmaceutical manufacturers produce and ship prescribing information (PIs) with each drug package. Considering the modest incremental costs associated with adhering PPIs to packages along with the PI, it is clear that the resources needed to print leaflets that serve public safety and complement product marketing would not be significant.

   - Unit-of-use formats represent a cost-effective means of attaining the Year 2006 goals. If these formats were more readily available from pharmaceutical manufacturers, pharmacist work time needed to repackage drugs in the pharmacy would be significantly reduced, and PPIs could be adhered directly to the unit-of-use container by the manufacturer – further reducing pharmacist work time currently spent printing out leaflets. These time saving solutions would allow pharmacists more time to spend with patients, and help reduce the shortage of pharmacists currently facing the United States. Additionally, pharmacies would no longer need to contract with third-party vendors for patient leaflets.

5. ***The technology does not exist to produce leaflets that are useful, particularly with regard to legibility by FDA standards.***

   As printers to the world's leading pharmaceutical manufacturers, PPLA member companies have developed folding and formatting solutions to address any number of applications. The technology does in fact exist through equipment and systems that are already in place to employ economies of scale in the production of legible, consistent and FDA-compliant leaflets in quantities and formats that scale to manufacturer and distributor requirements.

6. ***Electronic alternatives make more sense as a patient information resource than printed leaflets.***

   The PPLA contends that online information best serves as a complement to printed patient information, not as a substitute. First and foremost, FDA has no authority to regulate the use of electronic databases in pharmaceutical dispensing sites. As a result, the public has no guarantee that such systems will operate properly. Moreover, as stated by Linda Golodner, Chair of the National Council on Patient

Information and Education (NCPIE), during the July 31 public meeting, electronic resources "are no substitute for printed information."

Pharmacy and hospital healthcare personnel must always have access to critical prescription drug information. This access cannot be guaranteed by electronic means for a number of reasons, among them the fact that computers are subject to power failures, hackers and even terrorist attacks. In addition, many healthcare workers operate in environments where electronic systems are not available. Field doctors, pharmacists working from so-called mobile pharmacies, and those in rural areas of the country cannot be effectively served by electronic means solely.

It should also be noted that efforts by PhRMA to develop a nationwide electronic system are still in a very embryonic phase of testing. The time needed to fully test and implement such a system will likely be measured in years, if not decades, and there are no assurances that such a system will ever be proven to function adequately.

To this point, the PPLA notes that each dispensing site in the United States would have to be outfitted with at least several hundred dollars worth of equipment for the PhRMA "paperless labeling" initiative to achieve its goals. While PhRMA has contended that this equipment must be provided free-of-charge to every dispensing site, to the PPLA's knowledge, no entity has been identified to take responsibility for purchasing and maintaining this equipment.

It is not realistic to consider PhRMA's "paperless labeling" initiative as any type of means to FDA's end regarding the Year 2006 goal for useful printed patient information distribution with 95 percent of prescriptions filled. Doing so can only delay Year 2006 objectives and should be soundly rejected by FDA. It is entirely possible that the envisioned system is a pipedream that will never be fully realized.

Advantages and Efficacy of Mandatory PPIs Relative to the Year 2006 Goal

Having addressed the various objections to mandatory FDA-approved, manufacturer-produced printed patient information, the PPLA respectfully offers the following benefit and efficacy points relative to mandatory PPIs for all prescription drugs:

- PPIs can be designed to meet all the requirements for useful patient information detailed in the Keystone Action Plan. Indeed, Dr. Svarstad noted in her study review on July 31 that the few PPIs that were encountered in the study rated highest in meeting the usefulness criteria.

- PPIs can be imprinted with barcodes containing the product's National Drug Classification (NDC) code – a goal supported by FDA for Rx and OTC products intended for distribution to healthcare facilities – as well as lot number, and manufacturer-provided expiration date.

- Implementing this existing, proven patient information technology makes the manufacturer the paramount drug information source, which is desirable to manufacturers according to PhRMA. It also prevents drug information from being changed onsite by the pharmacist, as often occurs today according to the National Association of Chain Drug Stores.

- Requiring that PPIs be attached to pharmaceutical packaging – especially unit-of-use formats – will make it significantly more difficult to produce counterfeit medications.

- Consumers deserve drug product information that is at least on par with that provided for packaged food, and over-the-counter drug products. No lesser standard should apply to prescription drugs where the possibility of patient injury or death is usually far greater.

- With mandatory PPIs for all prescription drugs, useful patient information would be provided at the dispensing site, a key factor cited by several participants at the July 31 hearing.

- For consumers with literacy and visual challenges, the advantages of PPIs are significant. Printing technology can readily incorporate color, graphics and other visual cues that facilitate comprehension and help protect against mistaking a medication for a similar, look-alike or even counterfeit product. These advantages come into play in all distribution channels, not just those employed in pharmaceutical distribution sites.

- Consumers in possession of manufacturer-provided, FDA-approved leaflets are more likely to use the information, increasing both patient safety and drug compliance. Many commented at the July 31 hearing that – with regard to credibility and patient appreciation – there is no comparison between PPIs and a leaflet stapled to a pharmacy's paper bag containing an amber vial.

- Dr. Svarstad's study showed that patient literature was being distributed with 89 percent of prescriptions filled for some very common drugs. Even with 89 percent as the current base level, achieving 95 percent distribution is likely unobtainable by 2006. By employing the approaches recommended by the PPLA, the success rate for distributing useful patient information can realistically reach 100 percent.

Conclusions and Supplemental Information

The voluntary approach to providing useful printed patient information has been a failure, and has provided a direct link to increases in patient risk and healthcare costs.

In fact, after reviewing the results of the 2001 University of Wisconsin study, the FDA's own Drug Safety and Risk Management Advisory Committee urged the Agency to exercise its authority to take over this critically important task from private industry. The PPLA strongly concurs. Key risk information available with every prescription will not be consistently, comprehensibly and legibly provided unless FDA compels manufacturers to take the lead.

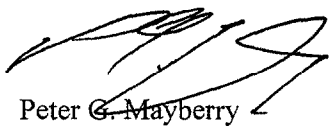
The PPLA also shares the view of the AARP, as voiced on July 31 by John Rother, AARP Director of Policy and Strategy, that food labeling is a good example of outcomes when private industry is entrusted to voluntarily implement full disclosure to consumers. Mr. Rother observed that manufacturers failed to provide comprehensive and consistent nutritional information about packaged foods until FDA required them to do so. As stated earlier in these comments, no lesser standard should apply to prescription drugs, which can be lethal if used incorrectly.

The PPLA submits its fact sheet, entitled "Data Correlating Improved Risk Management and Public Benefit to Useful Printed Patient Information for Prescription Drugs," as supplemental information to FDA. Most of the data in this fact sheet are derived from FDA's own research and review of the literature. In our opinion, these data make a compelling case for the urgent necessity of mandatory FDA-approved literature each time a patient fills a prescription.

In closing, the PPLA wishes FDA to know that we stand ready to assist the Agency in any efforts undertaken to glean useful consumer information in the form of PPIs or Medication Guides from existing PIs. As we noted during the public meeting, it may be beneficial for FDA to convene a work group comprised of Agency officials, learned intermediaries and literacy experts to address the task of developing PPIs or MedGuides, based on PI information, for drugs currently lacking them.

The PPLA thanks FDA for this opportunity to comment on the status of useful printed patient information. Please do not hesitate to contact me if you have questions about the PPLA's registration to present at the meeting. Alternatively you may contact my colleague, Alice Ducq at 703/538-5799, or via e-mail in care of amducq@aol.com.

Sincerely,



Peter G. Mayberry
Executive Director