

Comment to the Docket

“Electronic Distribution of Prescribing Information for Prescription Products”
FDA Public Hearing Convened April 27, 2007

FDA Docket Number 2007N-0114

Prepared and Submitted by the
Pharmaceutical Printed Literature Association
131 E. Broad Street, Suite 206
Falls Church, Virginia 22046

June 22, 2007

On behalf of the Pharmaceutical Printed Literature Association (PPLA) we thank the U.S. Food and Drug Administration (FDA) for this opportunity to submit further comment on the issue of “Electronic Distribution of Prescribing Information for Prescription Products” (FDA Docket Number 2007N-0114). PPLA Executive Director Peter Mayberry was a witness at the April 27, 2007, public hearing FDA convened on this issue and offered a brief overview of our views, as well as our concerns that FDA may be embracing electronic alternatives to tried-and-true, broadly-accepted, inexpensive technology that is currently required under Federal law. We also expressed our concern that the Agency would be ceding the broad Federal jurisdiction given to it by Congress to a system of separate state jurisdictions and/or private entities if it were to allow electronic alternatives to existing requirements.

In these comments we address several issues that were raised during the public hearing, and further articulate our belief that existing regulations regarding prescribing information should not be altered.

The PPLA contends that, with regard to drug products, FDA has two cornerstone responsibilities given to it by Congress under the Food, Drug, and Cosmetics Act (FDCA). These responsibilities are to ensure that all drug products offered for sale in the United States are: 1) manufactured and packaged according to legal standards; and 2) safe and effective when used as labeled.

The FDCA gives FDA virtually no authority, however, over the practice of pharmacy – which is left to the individual states – and Congress precludes FDA from involving itself in the practice of medicine.

Generally speaking, therefore, FDA’s authority over prescription (Rx) and over-the-counter (OTC) drug products basically ends at the manufacturers’ door.

In carrying out both of these responsibilities, FDA has relied for decades on regulations¹ that require Rx drug manufacturers to include “prescribing information²” with each container of Rx product they ship. This has been the historically-proven standard for ensuring FDCA requirements that sufficient care has been taken to guarantee that qualified professionals will always have information needed – under every conceivable distribution circumstance – to dispense product correctly and provide consumers with adequate counseling about the drug.

As a document, the PI is written for professionals – pharmacy personnel and physicians, mostly – who are legally allowed to dispense Rx drugs. The information contained in the PI is prepared by the Rx manufacturer and approved by FDA. This existing requirement is a time-honored, simple and inexpensive means of guaranteeing U.S. consumers that the most critical information regarding Rx drugs has been provided by the manufacturer with each and every container that leaves the manufacturing facility. This, in turn, assures the

¹ 21 CFR 201.100(c)(1)

² The terms “prescribing information” and “package insert” are basically used interchangeably in industry, and both are commonly referred to as a “PI.”

general public that those who dispense medications can provide adequate counseling based on consistent, reliable, non-promotional information that has been approved by the United States government.

During the April 27 public hearing, FDA Deputy Commissioner and Chief Medical Officer Dr. Janet Woodcock indicated the Agency might be on the verge of considering regulatory changes that, one day, would eliminate the need for manufacturers of Rx drugs to ship PIs with all of their products. Specifically, according to the transcript from the public hearing, Dr. Woodcock said: “FDA is committed to facilitating transition to a world of electronic information and capitalizing on the efficiencies an electronic environment has to offer.”

Shortly thereafter, in a presentation by the Pharmaceutical Research and Manufacturers of America (PhRMA, a trade group that represents U.S. manufacturers of Rx products) it was noted that a primary goal of PhRMA’s *paperless labeling* initiative – which has been underway since 1998 – is to “Replace paper package insert.”

While agreeing that the availability of electronic information offers a number of benefits to U.S. consumers and the healthcare system in general, the PPLA asserts that allowing printed PIs to be replaced by electronic alternatives is: 1) contrary to public interest; 2) unnecessary; and 3) reckless.

We further contend that FDA’s stated interest in “facilitating transition to a world of electronic information” has already sent a chilling message to PPLA members who are currently considering investment decisions needed to comply with FDA regulations on PI formatting requirements that were finalized just 18 months ago.³

Public Interest

As the sole Federal agency tasked with oversight of the pharmaceutical manufacturing industry, FDA has unique responsibility for ensuring that the public interest is served when it comes to drug safety. This responsibility begins with the drug approval process and continues through the entire lifespan of every Rx drug product offered for sale in the United States. Requiring that Rx products be shipped with printed PIs is a major part of this responsibility since it guarantees that those who dispense drugs have been provided with adequate and reliable information regarding proper use, cautions, etc.

If FDA were to eliminate this requirement and allow manufacturers to simply make the PI available electronically, the Agency would cede its responsibility under the FDCA and transfer authority over product information to entities over which the agency has absolutely no jurisdiction.

³ “Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products,” U.S. Federal Register January 24, 2006 (pp. 3922-3997)

This issue is succinctly detailed in a legal brief submitted to the PPLA by one of its member companies:

Congress specifically addressed the issue of electronic dissemination of prescription information for health care professionals in section 21 of the United States Code, where it allowed labeling for prescription *devices* (emphasis supplied) intended for health care professionals, or in health care facilities, to be made electronically, if manufacturers afford health care professionals the opportunity to request labeling in paper form at no additional cost.

Clearly, having specifically addressed the issue of electronic dissemination of prescription information for devices, if Congress had intended to allow for the electronic dissemination of prescribing information accompanying prescription drugs under any circumstances, it would have said so. Congress specifically recognized and addressed the issue of electronically conveying prescribing information for devices, but was and remains silent on the same issue with regard to prescription drugs. Congressional silence under these circumstances cannot be construed as unintended or an oversight, but rather, must be construed as meaningful, intentional, and the will of Congress.

Moreover, based on the Tenth Amendment to the United States Constitution, pharmacies are subject to state and not Federal regulation. Thus, the states, and not the Federal government license pharmacists. Congress recognized this principal in section 21 of the United States Code, where it provided that pharmacies operating in conformance with state laws are exempt from FDA inspection.

While FDA in section 21, part 11 of the Code of Federal Regulations has declared its authority to inspect computer systems that transmit electronic records, Congress has specifically denied FDA this authority, as noted above, with regard to state regulated pharmacies.

Thus, again, Congress did not intend to grant FDA the authority to require state regulated pharmacies to deploy and maintain a computer system for the purpose of disseminating literature for health care professionals.

Unnecessary

The PPLA contends that it is unnecessary to substitute printed PIs with electronic alternatives. As more and more information about Rx drug products becomes available over the Internet and other electronic data sources, those who prefer these sources of information will undoubtedly have ready access to them in the years to come. But this does not mean there is any compelling reason for FDA to eliminate the requirements spelled out under 21 CFR 201.100(c)(1).

During the April 27 public hearing, and at other times in the recent past, those who support “paperless labeling” have generally argued that a paperless system provides four

distinct benefits: 1) electronic PIs are never out of date; 2) electronic PIs cannot become separated from Rx drug containers; 3) elimination of printed PIs would speed new drug launches and facilitate approval of new indications; and 4) electronic PIs would lower healthcare costs because Rx manufacturers would not have to pay for the preparation of printed PIs. It was also repeatedly asserted at the public hearing that healthcare professionals typically do not consult printed PIs.

The PPLA contends that printed PIs reasonably guarantee that critical information is readily available to those who dispense Rx drugs and counsel consumers on how those drugs should be taken and stored. With regard to outdated information contained in printed PIs, we note that, to our knowledge, there has been no evidence offered by PhRMA or any individual Rx drug manufacturer to back up claims that information contained in printed PIs is routinely out of date.

Moreover, if FDA is truly concerned about the timeliness of information contained in printed PIs, the PPLA has repeatedly recommended that bar codes be incorporated into PI formatting requirements such that any information that is not on the print PI – or differs from what appears on the print PI – can be easily identified by healthcare professionals when they dispense Rx drug products.

With regard to the argument that printed PIs can become separated from the original container and, therefore, are useless to healthcare professionals, the PPLA questions, again, whether this concern is based on anecdotal observation or if it is a real problem. And to the extent FDA is legitimately concerned about this issue, we note that numerous actions could be taken by the Agency short of allowing Rx manufacturers to replace printed PIs with electronic alternatives as the optimal solution.

There have been numerous advances in the printing industry over the past decade such that it can be virtually impossible to accidentally separate a PI from the container to which it has been adhered. The PPLA welcomes an opportunity to discuss these advances with FDA, and provide specific examples, should the Agency be interested.

As for arguments that electronic PIs would speed drug products to market faster and facilitate indication changes, the PPLA notes that negotiation of PI language between FDA and Rx manufacturers often comes near the end of the Agency's approval processes. For obvious reasons, printed PIs cannot be prepared until these negotiations have concluded. But it is important for FDA to realize that the printing industry which serves Rx manufacturers is extremely competitive and PPLA members pride themselves on their abilities to provide materials to their customers as quickly as possible.

To the extent that delays occur in shipments of new drug products – or products that receive an approved new indication – due to the time needed to print an approved PI, these delays tend to be extremely short.

Lastly, with regard to savings that could be achieved if Rx manufacturers were allowed to stop shipping print PIs with their products, the PPLA offers several observations. In the

first place, during his April 27 testimony Peter Mayberry drew a reasonable analogy that allowing Rx manufacturers to stop shipping PIs so they could save money would be akin to allowing a cruise line to do away with life rafts and/or life jackets for the same reason. Simply stated, it would be a “penny wise and pound foolish” approach to cost reduction.

The PPLA further notes that Ms. Karen Kistler of Genentech testified on April 27 that each printed PI for two of her company’s products, Avastin and Rituxan, cost approximately \$0.35 to produce. She further testified that most other print PIs cost \$0.03-\$0.12. She also explained that the PIs required for Avastin and Rituxan are especially big due to the amount of information required by FDA.

According to the best information available to the PPLA, the average wholesale prices for these two drugs are:

Avastin 100mg	\$687.50/vial
Avastin 400mg	\$2,750.00/vial
Rituxan 10mg/ml	\$608.69/10 ml vial
Rituxan 10 mg/ml	\$3,043.29/50 ml vial

With all due respect, the PPLA finds its somewhat disingenuous to imply that a single 35 cent PI, shipped in a carton that could contain multiple vials, would amount to an economic burden for a product that, at a minimum, costs more than \$600 and, at maximum, runs more than \$3,000 *per vial*.

Even with less expensive Rx products, the PPLA strongly urges FDA to consider these miniscule costs against the tremendous benefits and assurances provided by printed PIs.

Reckless

The PPLA contends that it would be reckless to entrust PI information exclusively to electronic sources. To this point, we reiterate that printed PIs are especially critical in emergency situations.

Over the past decade alone, the United States has witnessed a massive terrorist attack on our homeland, the long term dislocation of millions of people due to hurricanes and other weather events, a massive power outage that afflicted vast amounts of our country, and numerous other calamities. During each of these events, sole reliance on electronic PIs would most definitely not have been in the best interests of the general public. And most recently, FDA should note that concerted attacks on computer systems have become a tactic for terrorist organizations as reported on page A-1 of the May 19, 2007, edition of the *Washington Post*.⁴

Moreover, if FDA allowed electronic PIs to substitute for printed PIs, the PPLA contends that the Agency would have no statutory ability to, among other things: 1) require that

⁴ “As societies become increasingly dependent on computer networks that cross national borders, security experts worry that in wartime, enemies will attempt to cripple those networks with electronic attacks.”

dispensing facilities maintain equipment needed to view electronic PIs; 2) set performance standards or validation protocols for equipment needed to view electronic PIs; or 3) mandate that back up systems be in place to ensure that printed PIs are available in times of power outages or other calamity.

Conclusions

Just 18 months ago, FDA issued the most sweeping format changes to PIs in more than 25 years. As FDA is aware, these changes have resulted in some larger PIs and, as Ms. Kistler testified, it is a fact that new machinery will be needed for our industry to adequately fold PIs that meet the new requirements. It would be tremendously helpful to our industry, therefore, if FDA would clarify its view on a possible timeline for the “transition” that Dr. Woodcock referred to on April 27.

Through these comments, we hope to convince FDA that the Agency should continue promoting electronic dissemination of Rx drug information. But we also contend it is unnecessary and unwise to consider any regulatory changes for existing PI requirements.

Again, we thank FDA for this opportunity to express our views.

Please feel free to contact Peter Mayberry, PPLA Executive Director, should you have any questions or need any additional information related to these comments.