



January 22, 2014

The Honorable Margaret Hamburg, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

The Honorable Sylvia Matthews Burwell
Director
Office of Management and Budget
725 17th Street, NW
Washington, DC 20503

Re: FDA Rulemaking on Electronic Distribution of Content of Labeling for Human Prescription Drug and Biological Products

Dear Commissioner Hamburg and Director Burwell:

On behalf of the member companies of Biotechnology Industry Organization (BIO), we respectfully request that the Office of Management and Budget (OMB) issue the proposed Food and Drug Administration (FDA) regulation on the electronic distribution of prescribing information for human drugs and biologics. Once implemented, the rule will provide patients, providers, and caregivers with timely access to the most up-to-date prescribing information to inform the safe use of FDA-approved therapies.

BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

We note that the current regulatory agenda lists a goal of issuing FDA's proposed rule on *Electronic Distribution of Content of Labeling for Human Prescription Drug and Biological Products* in January 2014.¹ We understand that the rule was previously submitted to OMB for review, and we encourage OMB to help FDA meet that goal. BIO believes FDA has ample authority to enact paperless labeling, as Congress has not prescribed a specific mechanism of dissemination in the statute.

As a preliminary matter, it is also important to clarify the types of labeling printed for prescription drug products. The FDA-approved prescription drug product labeling, or the US Prescribing Information (USPI), is intended for Health Care Providers (HCPs) and prescribers, and contains a summary of FDA-approved scientific information to safely and effectively use or prescribe the prescription drug product according to its FDA-approved indications. The USPI's unfolded size often rivals that of a city roadmap, even being printed in 6 point font, on both sides. At least one copy of the USPI is required to accompany every container of drug product dispatched by a manufacturer into interstate

¹ See <http://www.reginfo.gov/public/do/eAgendaViewRule?pubId=201310&RIN=0910-AG18>, accessed on January 17, 2014.



commerce.² While sometimes multiple prescriptions can be filled from a single container dispatched from the manufacturer, to understand the volume of road-map sized USPI's printed annually, there were approximately 4 billion prescriptions written each year, from 2010 to 2012.³ In this modern era of ubiquitous information technology and real-time communication, this paper-based approach to the dissemination of important new medical information is wasteful, uneconomical, and inefficient. As such, BIO fully supports replacing the paper USPI with electronic distribution, with paper copies available upon request.

The FDA's proposed rule concerns only the dissemination of the USPI to healthcare professionals, and this is the subject of our letter. Other patient-oriented documents intended to help individual consumers understand a drug or biologic's benefits and risks, but that are not within the scope of the proposed rule, may include a Medication Guide (MedGuide), Patient Package Insert (PPI), Consumer Medication Information (CMI), FDA's new Patient Medication Information (PMI) Initiative, and any other documents or instructions created by the dispenser (*e.g.* the prescriber or pharmacy). In addition to electronic dissemination of the USPI, BIO also supports digital distribution and posting of the PMI in a centralized online repository so that patients and providers can access both professional and patient-oriented labeling in a more efficient manner.

In light of the evolution on information technology over the last thirty years, 21st century health care professionals have a growing expectation to access digital healthcare information. E-labeling is a proven solution that will have meaningful advantages for the public health and will reduce waste to benefit the environment.

A. Public Health Benefits of Paperless Labeling:

Paperless labeling will improve patient safety as health care providers (HCPs) will have access to the most recent FDA-approved US Prescribing Information (USPI), detailing a medicine's safety, efficacy, and conditions of use, in a format that can be updated in a matter of days rather than weeks or months. Currently, with paperless labeling, when the USPI is revised to include new safety information, there may be substantial lag time before the HCP has access to the new information because of the existing inventory of product with the old labeling in the supply chain.

With the integration of Electronic Medical Records (EMRs) in the health care system, HCPs, including pharmacists, are accessing information on prescription drugs via electronic means, whether in urban or rural settings and are relying primarily on electronic media for their information. It is important that they have the most updated information when making prescribing decisions.

² 21 CFR 201.100.

³ IMS Institute for Healthcare Informatics, *Declining Medicine Use and Costs: For Better or Worse?*, May 9, 2013. Available at: www.IMSheath.com.



The availability of paperless labeling in a standardized format, such as the National Library of Medicine's (NLM) DailyMed website's Structured Product Labeling (SPL) standard, enables incorporation of the most recent up-to-date labeling into EMRs. Manufacturers currently provide revised labeling in SPL format to the NLM within 14 days after obtaining approval. Additionally, pharmaceutical companies are committed to providing hard copies to HCPs on a timely basis when requested by the HCP.

B. Environmental Advantages of e-Labeling:

E-labeling provides a 'green' solution protecting limited natural resources. As noted above, with the integration of EMRs most HCPs and local pharmacies access up-to-date labeling electronically, and paper versions are usually discarded. Use of e-labeling not only saves natural resources, but also eliminates additional waste in limited landfills and reduces paper mill waste streams.

C. Positive Economic Impact:

Additionally, there are significant cost savings associated with e-labeling that will generate a positive economic impact. For example, BIO members report that each midsize pharmaceutical or biotechnology company could potentially save over 4-5 million dollars per year through electronic dissemination of the USPI. This estimate is based on the actual printing and paper costs, as the expenditure on paper alone is approximately 30% of the entire cost. This represents significant financial resources that would be better applied towards the research and development of new therapies for unmet medical needs.

D. Misconceptions around Paperless Labeling:

In discussions around paperless labeling, a number of misconceptions have been voiced publically. BIO feels it is important to address these concerns so that both sides of these issues are carefully evaluated as part of the rulemaking process.

1. *"Patient safety could be compromised if paper drug labeling information is not available."*

The USPI is intended for healthcare professionals that prescribe, administer, and dispense drugs. The USPI is not intended for *any* constituency except those who directly handle drugs in the original packaging, such as pharmacists, physicians, and nurses, for example. HCPs are even more likely to have access through e-labeling as the USPI may be limited to the original packaging. This argument also ignores the potential harm to patient safety that can be posed by product administration based on an out-of-date paper USPI that does not reflect the most updated FDA-approved safety labeling.

2. *"The Internet is not always available, particularly in underserved populations in rural and low-income areas as well as foreign territories where the military is deployed."*



HCPs, including pharmacies across the United States, including low-income areas and in the military, have internet access. Out of a total of 407 pharmacists recently surveyed, only 6% reported using paper resources exclusively to retrieve prescribing and drug information. Most other pharmacies (93%) reported using either an electronic resource or both electronic and paper resources (1% of pharmacists did not know what kind of resource they use).⁴ Additionally, in a separate study, seventy-seven and a half percent (77.5%), or 31 out of 40 surveyed, thought that dissemination of the prescribing information should change from a paper form to an electronic form.⁵

Electronic labeling will also help to accommodate new technologies and formats that many stakeholders may feel more comfortable with, such as smart-phones, tablets, and links embedded within electronic medical records. Furthermore, electronic labeling will allow HCPs to search for and find needed information quickly, rather than time-consuming search through the 'road-map' sized paper copy. As stakeholders note in the Government Accountability Office (GAO) report, "relying on electronic drug labeling as a complete substitute for paper labeling could help ensure that physicians, pharmacists, and patients have the most current labeling in a more-user friendly form...."⁶

3. *"There is no data to suggest the elimination of paper drug labeling would be beneficial to public health."*

To be clear, the USPI labeling is not proposed for elimination, only its dissemination in paper form unless specifically requested. It is indisputable that patient safety would be at risk if an HCP treated a patient on the basis of an outdated paper USPI, which would not list a major safety change that has been updated prior. For example, if new information contraindicates use of a drug in a certain patient population and that information is delayed in getting to HCPs, then those HCPs can make uninformed prescribing decisions and patients may be put at risk.

4. *"FDA lacks the authority to require the complete replacement of paper labeling for prescription drugs."*

As of 1962, Congress gave the FDA authority to determine what constitutes "Labeling" and gave FDA latitude to determine how prescription products should bear adequate directions for use (*i.e.*, Labeling).⁷ In recent testimony to the House Energy and

⁴ Ho Y-X, Chen Q, Nian H, et al. (2013) An assessment of pharmacists' readiness for paperless labeling: a national survey. *J Am Med Inform Assoc*, doi:10.1136/amiajnl-2013-001654.

⁵ Drug Information Journal, *Taking the Package Insert into the Electronic Age*, Vol. 36, 2002, p.432.

⁶ Government Accountability Office, *Electronic Drug Labeling: No Consensus on the Advantages and Disadvantages of Its Exclusive Use*, July 2013, p. 13, <http://www.gao.gov/assets/660/655760.pdf>.

⁷ "[W]here any requirement of [labeling bearing adequate directions for use], as applied to any drug or device, is not necessary for the protection of the public health, the Secretary shall promulgate regulations exempting such drug or device from such requirement..." 21 USC §352(f)(2). See also, 62 Fed. Reg. 64073, 64076 (Dec. 3, 1997) ("[T]he requirement that products bear labeling with adequate directions for use [21 CFR 201.100] is met by inclusion of the products' FDA-approved professional labeling (package insert or product manual) that



Commerce Committee, Dr. Janet Woodcock, FDA's Director for the Center for Drug Evaluation and Research (CDER), testified that "I have long supported this....My understanding is, this requires rulemaking. The fact is that we are planning to issue a rule is on our agenda, and we plan to issue a rule this year, we would hope, a proposed rule."⁸

5. *"The Federal Food, Drug and Cosmetic Act states that drug labels need to be 'written, printed, or graphic matter,' that should also be 'upon the immediate container of any article.'"*

"Labels" have a different statutory definition than "Labeling". Labeling need only "accompany" the article and "accompanying" has an expansive meaning.⁹

6. *Shifting to electronic labeling could increase the cost burden for community pharmacists who would have to print labeling on request.*

It is important to note that the USPI is intended for HCPs and when asked, a pharmacist will provide a copy of the USPI. The USPI is not intended to be used to communicate benefits and risks to patients. As a matter of pharmacy practice, most pharmacies, including almost all chain pharmacies, now print *patient* friendly wording with each prescription filled, the software for which has to be purchased from a vendor.

7. *The GAO did not fully endorse e-Labeling.*

The results of the recent GAO report clearly state the advantages of electronic distribution of prescribing information.¹⁰ However, the report acknowledges that there was no clear consensus amongst diverse stakeholders on the use of e-labeling. This is likely due to the fact that the GAO was not mandated by the recently enacted Food and Drug Administration Safety and Innovation Act (FDASIA) to make formal

sets forth the uses for which the product has been approved/cleared as safe and effective"); 21 USC §352(f) and 21 USC §321(k) ("Adequate Directions for Use" in labeling must accompany the prescription drug product, unless exempted; there is no statutory requirement for physical attachment of USPI to any container); 21 USC §352(f)(2) (The Act gives the Secretary discretion to promulgate regulatory exemptions to labeling when statutory labeling "is not necessary for the protection of the public health"); 21 USC §352(f) (Prescription devices have statutory e-labeling exemption); 21 CFR 201.100(c)(1) (Current, FDA-approved USPI physically attached or included with primary prescription drug product container fulfills 21 CFR 201 regulations for labeling bearing adequate directions for use when repackaged or dispensed).

⁸ Woodcock, Janet. Statement to House, Energy and Commerce Subcommittee. *Securing Our Nation's Prescription Drug Supply Chain*, Hearing, 25 April, 2013 (serial 947 – 1005). Available at: <http://democrats.energycommerce.house.gov/sites/default/files/documents/Transcript-Health-Rx-Drug-Supply-Chain-2013-4-25.pdf>.

⁹ See *Kordel v. US*, 335 U.S. 345 (1948).

¹⁰ United States Government Accountability Office, *Electronic Drug Labeling: No Consensus on the Advantages and Disadvantages of Its Exclusive Use*, July 2013. Available at <http://gao.gov/assets/660/655760.pdf>.



recommendations.¹¹ Additionally, the scope of the report which extended beyond the focus of electronic distribution of professional labeling likely contributed to the ambivalent conclusions.

E. Conclusion:

E-Labeling will have clear benefit for the public health by providing timely access to new safety information and can make a positive impact on the environment by reducing unnecessary waste. BIO urges OMB to release the FDA's well-considered rule on *Electronic Distribution of Content of Labeling for Human Prescription Drug and Biological Products*.

BIO appreciates this opportunity to provide our perspectives and we would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

Andrew J. Emmett
Managing Director, Science and Regulatory Affairs
Biotechnology Industry Organization (BIO)

¹¹ Pub. L. No. 112 144, § 1140, 126 Stat. 993, 1126 (2012). FDASIA mandated GAO to examine the benefits and efficiencies of electronic drug labeling as a complete or partial substitute for paper labeling, the barriers to utilizing electronic labeling, and the impact on public health.