April 15, 2019

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA–2018-N-4735: FDA Agency Information Collection Activities: Proposed Collection; Comment Request; Safety Labeling Changes-Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act.

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA or Agency) for the opportunity to comment on the FDA's Agency Information Collection Activities (AICA): Proposed Collection; Comment Request; Safety Labeling Changes-Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (the Act).

BIO is the world's largest trade association representing 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.

In addition to the responding to FDA's specific request for input in the public docket on Safety Labeling Changes, Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act, we note that FDA's statements and estimates refer exclusively to electronic labeling (e-Labeling).[1] While this implies FDA's recognition that electronic labeling is the most accessible, expedient, efficient, and thus preferred method of providing labeling updates (particularly in the context of safety labeling changes which are deemed critical to a product's safe use), the failure to capture or mention the significant burdens incumbent on sponsors in the context of paper labeling renders the AICA activity incomplete and potentially ineffective.

Accordingly, our comments below provide additional context around the burdens associated with continued requirements for paper labeling, as well as a description of some of the public health benefits provided by e-labeling.

A. FDA's estimate of the burden of the proposed collection of information (including the validity of the methodology and assumptions used) are incomplete

[1]"FDA acknowledges that incorporating labeling changes into printed material included in drug shipments usually requires more time than incorporating changes to a Web site." Guidance, p. 13.

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The FDA issued a final guidance document in 2013 entitled, "Guidance for Industry: Safety Labeling Changes—Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act" that provided recommendations on updating sponsor's websites with new required safety information and indicated further guidance will be forthcoming for updating the required paper copies of the labeling. FDA has not yet issued any further guidance in this regard and sponsors are required to update paper copies of labeling accordingly.[2] Additionally, in October 2018, the SUPPORT for Patients and Communities Act[3] was enacted, which included provisions that expanded the scope of the initial provision, allowing the FDA to request changes in labeling due to reduced effectiveness. The AICA does not consider the increased number of potential labeling changes that may result from the SUPPORT Act provisions nor does it account for the resources required to update paper copies of required labeling.

Sponsors spend approximately 20-25 hours updating paper labeling, including managing quality control, graphic design, proofing, and final release of the final printed labeling every time a change is made to the labeling and the AICA fails to take this into account. Additionally, paper labeling with hard to read font also places significant burden on health care providers, and the health care system in general.

B. Implementation of e-labeling will inherently reduce the burden of the collection of information on respondents and improve patient safety

As implicitly acknowledged by the FDA, paperless labeling will improve patient safety as health care providers (HCPs) will have access to the most current FDA-approved US Prescribing Information (USPI), detailing a medicine's safety, efficacy, and conditions of use. Electronic access to this information offers not only the benefits of timely updating (i.e., a matter of days rather than months), but also provides a searchable, size-flexible format that arguably is most familiar to pharmacists and healthcare providers, who use resources like DailyMed and Drugs@FDA, and to which most commercial systems are linked. Currently, with paper labeling, when the USPI is revised to include new safety information, there may be a substantial delay before the HCP has access to the new information because of the existing inventory of product in the supply chain with the old paper labeling.[4] In stark contrast, the vast majority of product labels are already reported online in structured product label format at the National Library of Medicine's DailyMed website updated daily.[5]

The FDA-approved prescription drug product labeling USPI, is intended for HCPs, and contains a summary of FDA-approved 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 eight-point font on both sides, per the Physician Labeling Rule, 21 CFR 201.57. At least one copy of the USPI is

[2] 21 CFR 201.100, 201.306, 201.310, 606.121, 606.122, 610.60, and 610.61requires hard copies of labeling accompany the package.
[3] The SUPPORT for Patients and Communities Act
[4] Per Analysis of the Feasibility of Safety Labeling Changes Implementation Timeline," Final Report by Eastern Research Group, Inc., June 22, 2012, it can take up to 30 months for new labeling to appear with the finished product.
[5] FDA and NLM Memorandum of Understanding Regarding DailyMed

required, by regulation, not by statute, to accompany every container of drug product dispatched by a manufacturer into interstate commerce.

While sometimes multiple prescriptions can be filled from a single container, to understand the volume of USPI's printed annually, there are over 4.5 billion prescriptions written each year. In this modern era of ubiquitous information technology and real-time communication, this paper-based approach for dissemination of important new medical information is wasteful, uneconomical, inefficient, and potentially harmful to HPCs, patients, and caregivers. More importantly, the continued reliance on paper and the delays associated with paper labeling is contrary to a regulatory system that acts in the best interest of patients. This is supported by the fact that Internet usage over time has steadily increased: in 2018, 89% of adults use the internet.[6] Cell phones have increased access to the internet. In 2018 77% of Americans had a smartphone including over 9 out of 10 (92%) of Millennials.[7]

With the integration of Electronic Health Records (EHRs) 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. In fact, 98% of prescriptions are communicated via e-prescribing indicating access to online information.[8] The trends for both physicians to e-prescribe, and for pharmacists to rely on online sources of information regarding drugs have increased dramatically over the past few years. A few examples include the following:

- As of 2017, most office-based physicians (86%) utilized EHRs.[9]
- According to Surescripts, in 2017 most physicians used electronic prescribing methods (69%) and 98% of community pharmacies are able to accept electronic prescriptions indicating that a majority of HCPs have access to the internet.[10]
- Over 90% of all non-controlled prescriptions were delivered to the pharmacy electronically.[11]
- 98% of prescriptions are communicated via e-prescribing indicating access to online information.[12]
- The majority of pharmacies (93%) reported using either just an electronic resource, or both electronic and paper resources."[13]
- A national survey conducted in 2014, to assess the state of readiness for paperless labeling among a nationally representative sample of pharmacies, indicated that, as far back as 5 years ago, 79% of pharmacists felt that online availability of prescribing information would improve or greatly improve the adequacy of drug information.[14]

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[6] http://www.pewinternet.org/fact-sheet/internet-broadband/
[7] http://www.pewinternet.org/fact-sheet/mobile/
[8] https://surescripts.com/docs/default-source/national-progress-reports/2151_npr_2017_finalB.pdf
[9] https://dashboard.healthit.gov/quickstats/pages/physician-ehr-adoption-trends.php
[10] https://surescripts.com/docs/default-source/national-progress-reports/2151_npr_2017_finalB.pdf
[11] Id.
[12] https://surescripts.com/docs/default-source/national-progress-reports/2151_npr_2017_finalB.pdf
[13] PhRMA Paperless Labeling Study, Vanderbilt University School of Medicine, 2011
[14] Ho et al., An Assessment of Pharmacists' Readiness for Paperless Labeling: A National Survey, 21 JAMIA 43 (2014).

Considering the factors such as those listed above, and in the interest of ensuring the provision of instructions that meaningfully and effectively help ensure safe use of therapies, BIO fully supports replacing the paper USPI with electronic distribution, with paper copies available upon request.

As a result of the evolution of information technology over the last thirty years, 21st Century HCPs, patients and caregivers have a growing expectation to access digital healthcare information and the wide use of digital tools in many aspects of patient care. E-labeling is a proven solution that will have meaningful advantages for the public health. BIO recognizes FDA's challenges in implementing e-labeling; however, BIO believes FDA has ample authority to enact paperless labeling, as Congress has not prescribed a specific mechanism of dissemination. Notably, there is cross-industry support for the December 2014 proposed rule, "Electronic Distribution of Prescribing Information for Human Prescription Drug, Including Biologic Products."

BIO appreciates this opportunity to submit comments regarding FDA's FDA Agency Information Collection Activities: Proposed Collection; Comment Request; Safety Labeling Changes-Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/
Danielle Friend, Ph.D.
Director, Science and Regulatory Affairs
Biotechnology Innovation Organization