GPhA Overview and Assessment:

Food and Drug Administration’s Proposed Rule
Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products

January 2014
Executive Summary

Patient safety is the foremost concern for manufacturers of generic medicines, which is why both brand and generic companies comply with federal law and strict FDA labeling rules and regulations. Generic drug companies proactively participate with the FDA in ensuring the timeliness, accuracy, and completeness of drug safety labeling in accordance with current regulatory requirements, to ensure doctors and all healthcare professionals and patients have access to the most up-to-date information.

On November 13, 2013, the Food and Drug Administration (FDA) issued a proposed rule regarding Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products1 (Proposed Rule). FDA made it clear that it intends to establish “parity” between Abbreviated New Drug Application (ANDA) and New Drug Application (NDA) sponsors by requiring ANDA sponsors to submit Changes Being Effected supplements (CBE-0) to modify their labeling when they receive or otherwise obtain new safety-related information. The labeling changes are expected even though they will result in the generic drug labeling differing from the reference listed drug (RLD) labeling.

It is difficult to overstate the implications of the Proposed Rule on the generic pharmaceutical industry. The Proposed Rule creates the regulatory framework whereby multiple, different labeling, including different warnings, can simultaneously exist in the marketplace for the “same” drug. The confusion that will be created among health care professionals will undermine FDA’s longstanding, unwavering emphasis on consistency in drug labeling. The confusion that will ensue has obvious implications for public health, which FDA has not addressed in its Proposed Rule. FDA also did not conduct a robust cost/benefit analysis, and attempts to minimalize the potential that the Proposed Rule, if adopted, very likely will result in defensive labeling. FDA also failed to recognize that adoption of the Proposed Rule may result in under-adoption of safe and effective generic drugs that improve lives and reduce healthcare costs, fewer generic drugs coming to market, manufacturers withdrawing from certain markets, drug shortages, and increased expense of drugs – all antithetical to the basic purposes of the Drug Price Competition and Patent Term Restoration Act of 1984 (better known as the Hatch-Waxman Amendments to the Food, Drug, and Cosmetic Act (FDCA)).

Generic drug manufacturers are important participants in the pharmaceutical industry and participate in the pharmacovigilance process. However, the Generic Pharmaceutical Association (GPhA) cannot support a proposed rule that undermines public health merely to facilitate litigation against generic drug companies by the plaintiffs’ bar.

GPhA fully supports a streamlined, efficient process for updating safety information regarding the use of pharmaceutical products for health care practitioners and the general public. However, GPhA believes that the Proposed Rule does not conform to the statutory requirements for ANDAs as they relate to labeling and has serious concerns about disparate information being distributed to healthcare practitioners and the general public regarding potentially significant safety concerns. Since the passage of the Hatch-Waxman Amendments to the FDCA, generic manufacturers have fulfilled important pharmacovigilance responsibilities to protect the patients they serve. GPhA believes, however, that simple changes to the Proposed Rule can achieve all of FDA’s objectives related to efficient communication of important safety information in a more rational and coherent manner.

Introduction

Drug product labeling and patient safety have been major concerns since the turn of the twentieth century and were first addressed through federal legislation in 1906 with the Pure Food and Drug Act. Over the years, that concern has manifested itself in continual efforts to update legislation and implementing federal regulations with numerous amendments. In the early 2000s, amendments addressed safety in the form of product-specific patient leaflets and Risk Evaluation and Mitigation Strategies (REMS). More recently, the Supreme Court decisions *PLIVA, Inc. v. Mensing* and *Mutual Pharm. Co., Inc. v. Bartlett* focused attention on generic drug manufacturers and their inability to change their labeling to include additional or strengthened warnings of new safety concerns. The Supreme Court’s decisions acknowledged the clarity of the statutory language that requires a generic drug’s label to be the same as that of its reference listed drug (RLD) and prohibits changes even to strengthen the labeling that would vary it from the RLD. Subsequently, members of Congress and others have looked for ways to require generic drug manufacturers to revise their labeling to include new safety information independent of the RLD labeling.

The generic pharmaceutical industry performs pharmacovigilance activities related to adverse experience events involving their approved drugs. However, since the implementation of Hatch-Waxman, FDA has consistently stated that ANDA sponsors cannot distribute labeling with new safety information unless FDA has approved changes the innovator made to its labeling. Despite FDA’s longstanding position (stated as recently as July 2013 in a footnote to its “Guidance for Industry” Safety Labeling Changes - Section 505(o)(4) of the FD&C Act,2 it appears that FDA’s posture has now suddenly changed dramatically as evidenced by the Proposed Rule.

The Hatch-Waxman Amendments were designed to strike a delicate balance between the brand-name drug industry and the generic drug industry. That balance permitted generic drug applicants to rely on findings of safety and efficacy that were made with respect to an NDA as support for approval of the ANDA provided the proposed generic drug product was the “same as” the reference product upon which it is based, including in the content of the labeling. In turn, the brand-name drug industry received additional product protection through the award of periods of market exclusivity, patent term extensions, and patent protections.

Under the statute and regulations governing ANDA submission and approval, a generic drug product is required to maintain the same labeling as the RLD after ANDA approval, with limited exceptions. FDA’s Proposed Rule contemplates allowing ANDA applicants to submit changes to their labeling of their approved products that differs from the RLD labeling in order to reflect new safety information, absent an affirmative FDA approval of such a change in the RLD’s labeling, or a demand by FDA for all applicants of a specific drug product to make such a change in labeling. However, this proposed abandonment of the requirement of sameness in generic drug and reference listed drug labeling will lead to confusion in the marketplace for both patients and health care practitioners.

FDA states in its Proposed Rule that “[t]he Mensing decision alters the incentives for generic drug manufacturers to comply with current requirements to conduct robust postmarketing surveillance, evaluation, and reporting, and to ensure that the labeling for their drugs is accurate and up-to-date.” GPhA takes exception to that statement. First, the post-marketing reporting

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requirements for generic drug manufacturers continue to be in effect and were not changed by *Mensing*. Second, GPhA believes it is not the regulatory obligations that lead most of our members to “conduct robust postmarketing surveillance, evaluation, and reporting, and to ensure that the labeling for their drugs is accurate and up-to-date”; it is instead their desire to provide clear and meaningful information about their products to patients and health care providers. However, GPhA does recognize it is FDA’s role, as regulator, to ensure all drug manufacturers (both brand and generic) are meeting their obligations relative to established postmarketing surveillance requirements. Patient safety is the foremost concern of GPhA members and GPhA members are diligent in their responsibility to send adverse event reports to FDA.

The Proposed Rule would permit ANDA applicants to make CBE-0 changes to labeling and issue “Dear Health Care Provider” letters immediately upon submission of a CBE-0 – something the Supreme Court already stated the statute does not allow. The FDCA requires labeling to be the same as the RLD, and the preamble to FDA’s regulations implementing the Hatch-Waxman Amendments correctly explained that consistency between labeling of the RLD and ANDA not only is required by the statute, but also is essential to avoid confusion in the marketplace. Now, in the Proposed Rule, FDA is advocating for a scheme that would lead to exactly the confusion it has steadfastly worked to avoid for the past 30 years. FDA’s reasoning for its changed position – that the marketplace has changed since the passing of Hatch-Waxman as purportedly evidenced by the fact that now 84% of all drug products dispensed in this country are generic products – is flawed.

The Proposed Rule raises significant concerns for the generic drug industry, the country’s healthcare system, and the nation’s citizens. As written, the Proposed Rule could have a staggering impact on the future availability of low-cost generic drugs as well as increasing the number of instances during which life-saving drugs either are in short supply or are not available. The Proposed Rule is expected to create an environment in which some generic drug manufacturers will be forced to discontinue business in the United States. From a public health perspective, industry and FDA should work together to address any well-grounded public health concerns and develop a rational approach as needed. However, it is important to briefly review how injurious approaches in the Proposed Rule could impact health care in America.

In addition to the significant patient safety concerns presented, it is striking that FDA would propose a rule that will have the predictable effect of raising costs for drug therapies at a time when this country is focused on the need to further expand the accessibility of health care and reduce its accelerating costs. If the Proposed Rule takes effect for generic manufacturers, it will have the (expressly-intended) consequence of exponentially increasing litigation risk, burdening generic companies with additional regulatory obligations, and increasing the cost of drugs that already have been vetted by FDA through the rigorous NDA process, and safely marketed for years during the period of exclusivity for the NDA holder. Adoption of the Proposed Rule will inevitably impact the decision of generic pharmaceutical companies whether to enter the market with a specific drug in the first place, whether to cease manufacture and sale of drugs that are presently the subject of substantial litigation, or whether to remain in the market and pass through to consumers the additional cost of dealing with the ensuing nationwide litigation and increased regulatory demands. Indeed, litigation risks already have resulted in shortages of drugs necessary for important therapies, and that phenomenon will only increase as manufacturers are forced to conduct a substantially different economic analysis imposed by the Proposed Rule. The Proposed Rule also would lead to inefficiencies, such as multiple

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3 See 57 FR 17950, 17961.
manufacturers issuing multiple label changes for therapeutically equivalent drugs, further increasing the costs for the industry and provider and patient confusion.

A 2013 analysis by the IMS Institute for Healthcare Informatics, a division of IMS Health, a leading provider of market intelligence to the health care industry for more than 55 years, shows conclusively that the use of lower cost generic prescription drugs is a vital component to holding down the growth rate of health care spending. As the study shows, generic drug use has saved the U.S. health care system approximately $1.2 trillion over the past decade (2003 through 2012) with $217 billion in savings achieved in 2012 alone. Savings from newer generic medicines—that those that have entered the market since 2003—continue to increase exponentially, totaling $639 billion over the past 10 years. Those savings have allowed consumers in the United States, access to medications that they may not have been able to afford otherwise.

Proper use of medications is one of the most effective ways to mitigate and cure disease, thereby leading to patient comfort and well-being. Proposing regulations that will drive companies from the generic pharmaceutical sector will result in worsening public health outcomes. It is well established that cost is a critical factor in patient compliance with medication use. The total economic impact of medication non-adherence—which contributes to costly health complications, worsening of disease progression, and preventable utilization—has been estimated to be as much as $290 billion. More than one in 10 seniors in the America reported reducing use of their required medications because of cost.

Noncompliance with medications leads to a deterioration of the patient’s health, which can ultimately lead to a lower quality of life or even possibly death. Driving up the cost of generic drugs will unfortunately contribute to these situations, since fewer patients will be able to afford their prescriptions.

**Brief Overview of the Regulatory System for Brand-Name and Generic Drugs**

The FDCA controls the approval process for new drugs. Innovator manufacturers seeking FDA approval for new drugs are required to perform careful research, testing and clinical trials to gain FDA approval to market a new drug, and to ensure that its labeling is adequate. Under the congressional scheme for “innovator” drug manufacturers, innovator manufacturers and FDA act in partnership and share decision-making in preparing adequate labeling and warnings.

To ensure that generic drug manufacturers could enter the market to produce drugs less expensively, Congress expressly exempted them from the expensive, time-consuming, and ultimately repetitive clinical testing and trials that already had been performed on the innovator drug. In the place of such development and testing requirements, Congress established exclusive, unbending requirements for generic drugs. Through enabling regulations, those requirements include postmarketing reporting responsibilities to the FDA. The pertinent requirements to obtain approval are: (1) that the generic drug is the “same as” the approved innovator drug; and (2) that its warnings and labeling mirror those approved by FDA for the RLD.

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Likewise, extensive federal regulations address drug labeling, providing detailed requirements relating to the content and format of labeling for prescription drugs.\(^7\) The FDCA makes it unlawful to distribute a drug that is “misbranded,”\(^8\) and a drug will be considered misbranded unless “its labeling bears adequate warnings against use, where its use may be dangerous to health.”\(^9\) A prescription drug also can be considered misbranded if the labeling discusses unapproved uses of the drug or off-label indications. There are civil or criminal penalties for distributing misbranded drugs.\(^10\)

Section 505(j) of the Hatch-Waxman Amendments establishes the requirements for generic drug approval under the ANDA process.\(^11\) Specifically, the process begins with a requirement that the generic drug not be new or innovative.\(^12\) The 1984 House Report on the Drug Price Competition and Patent Term Restoration Act\(^13\) explains that “the focus of [§ 355(j)] is to provide [FDA] with sufficient information to assure that the generic drug is the same as the listed drug,” thereby obviating any need for duplicate testing for safety or effectiveness of the generic drug. Thus:

> [T]he manufacturer of a pioneer drug must conduct tests on humans that show the product to be safe and effective and submit the results in a new drug application (NDA). A manufacturer of a generic drug must conduct tests that show the generic drug is the same as the pioneer drug and that it will be properly manufactured and labeled.\(^14\)

As has been the case since the passage of the Hatch-Waxman Amendments, only the innovator, and not a generic drug manufacturer, can add to or strengthen a warning without first obtaining FDA’s approval. Upon doing so, the innovator must submit an NDA supplement to notify FDA, which will approve, modify, or disapprove the new warning.\(^15\) Likewise, FDA now can initiate labeling changes, including addition of warnings, if the Agency determines they are warranted on the basis of new information received after NDA approval.\(^16\) In most cases prior to May 2000, even if FDA already had approved changes in the innovator labeling, it still could require a generic drug manufacturer to submit a supplement for prior approval before allowing the generic drug manufacturer to utilize the changed labeling. After that date, if the innovator has received approval for a change in labeling, the Office of Generic Drugs (OGD) allows the ANDA sponsor to revise its label, only to comply with the exact change approved for the innovator by the submission of a CBE Supplement.\(^17\)

\(^{7}\) See 21 C.F.R. §§ 201.56 and 201.57. See also 21 C.F.R. pt 201.

\(^{8}\) 21 U.S.C. § 331(a).

\(^{9}\) Id. §§ 331(a), 352(f).

\(^{10}\) Id. § 333.

\(^{11}\) 21 U.S.C § 355(j).

\(^{12}\) See § 321(aa) (ANDA must “rel[y] on the approved application of another drug with the same active ingredient to establish safety and efficacy.”)


\(^{15}\) See 21 U.S.C. § 356a(d); FDA Guidance for Industry - Changes to an Approved NDA or ANDA (November 1999) (FDA Guidance November 1999) at 24-25 and Revision 1 to that Guidance, issued April 2004 at 24-26. See also 21 CFR § 314.70, which the FDA interpreted in similar fashion. Please note that the FDA, on April 8, 2004, issued a Final Rule (69 FR 18728) that revised 21 CFR § 314.70(c), and such rule took effect on June 22, 2004).

\(^{16}\) See Id. §§ 200.5 and 314.

Previous FDA Positions on ANDA Labeling Contrary to the Proposed Rule

In the preamble to the original Proposed Rule establishing the ANDA regulations (54 FR 28872-28942 July 10, 1989), FDA specifically notes that “changes in labeling (such as new warnings or precautions) intended to address newly introduced safety or effectiveness problems not presented by the listed drug … do not fall within the limited exceptions in sections 505(j)(2)(A)(v) and … FDA does not believe it would be consistent with the purpose of section 505(j) of the Act, which is to assure the marketing of generic drugs that are as safe and effective as their brand-name counterparts, to permit the marketing of generic drugs with diminished safety or effectiveness and concomitantly heightened labeled warnings.”18 That position is consistent with GPhA’s position that new warnings or precautions should be added to generic drug labeling in concert with changes to the RLD labeling regardless of who initiates the proposed labeling change, and that FDA is the appropriate arbiter to determine the specific labeling content.

The importance of consistency between the labeling of brand-name and generic drugs was reinforced by FDA in its response to comments to the proposed ANDA rules. The commenters requested that ANDA applicants should be permitted “to add contraindications, warnings, precautions, adverse reactions, and other safety-related information” not found in the RLD labeling. In publishing the final ANDA rules (57 FR 17950 – 18001), FDA responded by saying, “[c]onsistent labeling will assure physicians, health professionals, and consumers that a generic drug is as safe and effective as its brand-name counterpart.”19 In this same section, FDA goes on to say, “[a]fter approval of an ANDA, if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised.”20

There are other various requirements a generic pharmaceutical manufacturer must meet for approval depending on the circumstances. For example, subsection 505(j)(2)(A)21 requires an ANDA to show:

• the conditions of use on the proposed labeling for the generic drug are the same as those approved for the listed drug,22 excepting only indications covered by a patent or subject to exclusivity protection under § 505(j)(5)(D) of the Hatch-Waxman amendments.23

• the proposed labeling is the “same as” that of the listed drug, except for differences reflecting (i) that the drug is produced or distributed by a different manufacturer; or (ii) FDA approved variations in the generic drug’s administration, dosage form or strength.24

The Hatch-Waxman Amendments to the FDCA and FDA’s regulations provide that FDA cannot approve an ANDA if “information submitted in the application is insufficient to show that the labeling proposed for the [generic] drug is the “same as” the labeling approved for the listed

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18 [cite] (emphasis added).
19 [cite] (emphasis added).
20 [cite] (emphasis added).
21 http://www.fda.gov/ohrms/dockets/98fr/110102a.htm
23 See 21 C.F.R § 314.94(a)(8)(iv); see also 57 Fed. Reg. at 17,961.
drug [except for changes required because of differences approved under a 505(j)(2)(C) [suitability] petition or, because the [generic] drug and the listed drug are produced or distributed by different manufacturers.” Regulations also clearly state that the FDA can declare a drug misbranded if, after approval, a generic manufacturer fails to maintain a label similar to the approved innovator labeling.25

Generic drug manufacturers cannot add to or revise any warnings on the product labeling without the FDA’s express direction or prior approval of the innovator’s label.26 That prohibition applies even if the manufacturer of the innovator drug added or strengthened a warning without the FDA’s prior approval.27

The United States Supreme Court’s decision in PLIVA v. Mensing outlined the Court’s understanding that the FDCA requires “the warning labels of a brand-name drug and its generic copy must always be the same – thus, generic drug manufacturers have an ongoing federal duty of sameness.”28

In accordance with the requirements of the statute, FDA has maintained the position that labeling changes cannot be made unilaterally by a generic manufacturer.29 FDA expressly rejected public requests that ANDA applicants be allowed unilaterally to change or deviate from the labeling of the innovator drug to add contraindications, warnings, precautions, adverse reactions, and other safety related information.30 Throughout its implementation and enforcement of the Hatch-Waxman Amendments, FDA has admonished that “all labeling changes for ANDA products must be consistent with § 505(j) of the Act.”31 That admonishment appears, for example, in the November 1999 FDA Guidance and in the April 2004 Revision of that Guidance, as well as other documents and materials issued by FDA over the years. That admonishment was reiterated on January 16, 2008, in FDA’s Proposed Rule entitled Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics and Medical Devices32 which provided the following specific advice in regard to changes that are made under 21 CFR 314.70(c)(6)(iii):

CBE changes are not available for generic drugs approved under an abbreviated new drugs application under 21 U.S.C. 355(j). To the contrary, a generic drug manufacturer is required to conform to the approved labeling for the listed drug.33

That requirement was confirmed by the United States Supreme Court in Mensing,34 which held that generic drug manufacturers cannot use the CBE process to unilaterally strengthen their warning labels. However, despite those precedents, FDA is now attempting to provide for such label changes by ANDA holders in a manner contrary to law. Those changes surely will create confusion and harm in the marketplace among patients and healthcare providers alike.

25 Id. § 314.150(b)(10).
26 57 Fed. Reg. at 17,957, 17,961.
27 Pursuant to 21 U.S.C. § 356a and the November 1999 FDA Guidance, Revision 1 to that guidance (or the predecessor or revised regulation, 21 C.F.R. § 314.70).
29 21 C.F.R. § 314.70(c)(6)(iii).
31 FDA Guidances at 24.
33 21 CFR § 314.150(b)(10); see also 57 FR 17950, 17953 and 17961.
Other examples of FDA’s adherence to the sameness requirement for labeling that is mandated by the statutory language (and thus FDA’s statements in its implementing regulations) include the writings of Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research, in an FDA October 29, 2010 response to a petition submitted by Mylan Laboratories Inc.\textsuperscript{35} that stated:

> After an ANDA has been approved, the ANDA must continue to have the same labeling as the listed drug. As described in the Agency’s guidance for industry, Revising ANDA labeling Following Revision of the RLD Labeling (ANDA Labeling Guidance), approved changes in the listed drug’s labeling generally necessitate changes in the labeling of the ANDA referring to the listed drug. ANDA sponsors are responsible for ensuring that the labeling contained in its application is the same as the currently approved labeling of the listed drug.\textsuperscript{36}

The Solicitor General affirmed that requirement in a March 2011 Brief for the United States as Amicus Curiae Supporting Respondents: “FDA places ‘a very high priority [on] assuring consistency in labeling,’ so as to minimize any cause for confusion among health care professionals and consumers as well as to preclude a basis for lack of confidence in the equivalency of generic versus brand name products.”\textsuperscript{37}

**GPhA Concerns with the Proposed Rule**

In the Proposed Rule, FDA stated it “is proposing to amend its regulations to revise and clarify procedures for application holders of an approved drug or biological product to change the product labeling to reflect certain types of newly acquired information in advance of the FDA’s review of the change.”\textsuperscript{38} The Proposed Rule, according to FDA, would create parity among application holders with respect to such labeling changes by permitting holders of ANDAs to distribute revised product labeling that differs in certain respects, on a temporary basis, from the labeling of its RLD upon submission to FDA of a CBE-0 supplement. GPhA believes such a regulatory change is contrary to the clear language of the statute governing ANDAs that requires “sameness of labeling.”

GPhA supports a modification of the process that would explicitly allow generic firms to actively assist FDA in its determination that a change to labeling based on new safety information is warranted and in an efficient and prompt review of proposed changes by FDA. As noted above, the GPhA fully supports an expedited communication process through which FDA can notify both generic and brand-name drug companies, as well as healthcare practitioners of potential new safety information. GPhA does not, however, support a process that requires submission of independent CBE-0 supplements by ANDA applicants for proposed changes and differences in product labeling compared to the RLD (and compared to other ANDA applicants) while FDA assesses the changes.

\textsuperscript{35}Docket No. FDA-2006-P-0329, available at \url{http://www.regulations.gov/#!documentDetail;D=FDA-2006-P-0329-0007}.
\textsuperscript{36}Docket No. FDA-2006-P-0329, available at \url{http://www.regulations.gov/#!documentDetail;D=FDA-2006-P-0329-0007}.
\textsuperscript{37}See \url{http://www.americanbar.org/content/dam/aba/publishing/previewbriefs/Other_Brief_Updates/09-993_respondentamcuusa.authcheckdam.pdf}.
\textsuperscript{38}Docket ID: FDA-2013-N-0500, available at \url{http://www.regulations.gov/#!docketDetail;D=FDA-2013-N-0500}. 
Highlights of FDA’s Proposed Changes:

- The ANDA holders would be permitted to make CBE-0 changes to labeling for safety related changes and issue “Dear Health Care Provider” letters BEFORE such labeling is approved for the RLD;
- FDA will make the proposed safety information publicly available while the Agency is reviewing the information;
- Companies must submit conforming changes to the “Highlights of Prescribing Information” with labeling in the Physician Labeling Rule (PRL) format;
- ANDA holders must notify the RLD NDA holder of the proposed labeling change that is the subject of the CBE-0 (FDA will review changes to an ANDA when there is no marketed NDA);
- Upon approval of the labeling change for the RLD, all ANDA applicants would have 30 days to submit a CBE-0 supplement with conforming labeling; and
- FDA may take steps to withdraw approval of an ANDA if the generic drug labeling is no longer consistent with the RLD.

In general, the Proposed Rule would impose an obligation on ANDA holders to update product labeling promptly to reflect certain types of newly acquired information related to drug safety, irrespective of whether the revised labeling differs from that of the RLD. Yet, the Agency has acknowledged the difficulty in assessing postmarketing safety data\(^3\) noting that “interpreting postmarket safety data is complex, involving analysis of clinical data and detailed review of widely variable labeling statements for potentially relevant information, including ADE spontaneous reports, pertinent controlled clinical trials and epidemiologic studies, active surveillance efforts, estimates of drug usage and ADE reporting rates, estimates of background rates of adverse events, and other information.” Despite utilizing experts to assess new safety information, the probability of multiple varying CBE-0 submissions for the same drug product pending for an extended period of time while FDA reviews and assesses the proposed changes likely will result in increased and unnecessary confusion related to the safe use of drug products due to the complexity of interpreting that information. Consequences of such confusion include longer periods of time for review of differing labels, reverting back to original labels, and consumers losing confidence in the pharmaceutical industry.

Finally, the Proposed Rule will not enhance safety. The Proposed Rule jettisons the fundamental requirement of “sameness” and consistency and, instead, will lead to confusion and inconsistency in which the same drug has multiple, different labels conveying different safety information to health care professionals and the general public. Indeed, FDA acknowledged the “concern” caused by “differences in safety-related labeling for drugs” when multiple ANDA holders CBE-0 supplements, which could each differ from the other and from the labeling approved for the brand name equivalent, are simultaneously in the market.\(^4\) FDA states that it “recognize[s] that health care practitioners are unlikely to review product labeling for each of the generic drugs,” which would result in some health care providers having different information from others concerning therapeutically-equivalent drugs.\(^5\) **In short, FDA concedes that its proposal could lead to health care professionals paying less, not more, attention to the very labeling that the rule purportedly seeks to strengthen.**

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\(^5\) Id. at 67989.
Conclusions

The proposed rule includes revisions that would dramatically alter the current regulations governing generic drugs with respect to both when and how a labeling change would be required. GPhA is very concerned that multiple versions of critical safety information would lead to unnecessary confusion and uncertainty for prescribers and other healthcare professionals, with harmful consequences for patients. They also create an additional burden not anticipated in the business and compliance models of generic and biosimilar manufacturers and marketers.

Patients and healthcare practitioners must continue to have access to consistent, transparent information in order to best inform treatment decisions. The generic pharmaceutical industry will continue to work with the FDA and other stakeholders to make sure that any changes to labeling rules and regulations protect patient safety, align with federal laws, and do not hinder patient access to more affordable generic medicines.