STATEMENT OF BETH ZELNICK KAUFMAN

BEFORE THE SENATE JUDICIARY SUBCOMMITTEE ON ANTITRUST, COMPETITION, POLICY AND CONSUMER RIGHTS

JUNE 21, 2016

Chairman Lee, Ranking Member Klobuchar, and Members of the Subcommittee:

Thank you for inviting me here today. I am the Assistant General Counsel at Amneal Pharmaceuticals, a generic pharmaceutical manufacturer founded in the United States in 2002 that now provides jobs for more than 4,000 people both here and abroad. And while I am here today with examples that are specific to Amneal, please know that the problems and challenges I will share with you are real and pervasive across the entire generics industry.

Amneal and the Generic Pharmaceutical Association strongly supports the CREATES Act as an appropriate solution to a problem that my company and the larger generic and biosimilars industry is facing with increasing frequency: certain brand pharmaceutical manufacturers' abuse of FDA regulations designed to protect patient safety, called Risk Evaluation and Mitigation Strategies and commonly referred to as REMS. In addition, some brand manufacturers self-impose restricted distribution practices to limit market access to their product absent any FDA mandate.

Amneal and the larger generic industry are committed to ensuring that all Americans have access to safe, effective and affordable drugs and believe that FDA's REMS programs can and do serve a compelling public good – namely, the safe distribution and use of certain pharmaceuticals that have a higher risk profile. We do not support any policies that would jeopardize patient safety and any discussion or insinuation to the contrary you may hear today is simply an effort to distract us from the real issue we need to focus on: addressing the use of

REMS or other non-FDA mandated restrictions on drug supply that are designed – often times explicitly – to block lower cost generics and biosimilars from coming to market.

As you know, the Drug Price Competition and Patent Term Restoration Act (P.L. 98-417; 21 U.S.C. §355,) commonly referred to as Hatch-Waxman, has been incredibly successful at achieving its intended balance of supporting continued pharmaceutical innovation while achieving lower-cost generic competition. Since its enactment 32 years ago, generic drugs have produced trillions of dollars in savings for patients and payers alike. 88% of all prescriptions filled are now generic, saving the U.S. healthcare system $1.68 trillion over the last decade[1].

With that in mind, I believe today's discussion should begin with a fundamental question: do we believe in Hatch-Waxman Act or not? The CREATES Act answers that question affirmatively and remedies abuses that undermine Hatch-Waxman and the Biologics Price Competition and Innovation Acts (BPCIA) (P.L. 114-38, 42 U.S.C. § 262).

I. REMS ABUSES BLOCK GENERIC DRUG ENTRY

For the past 6 years I have seen first-hand, at two different generic companies how these ongoing abuses stifle generic development and delay market entry of affordable alternatives for America's patients. Our work in furtherance of this goal of lowering costs and improving access to medicines – a goal I know you share – is often frustrated by a brand hiding behind the veneer of a REMS, or self-imposed, restricted distribution program to limit or deny our access to samples.

For example, in December 2013 Amneal initially requested samples of one product subject to a REMS in order to conduct the required bioequivalence testing to bring a lower-cost competitor to market. Though it took nearly three years, a supply agreement was finally signed

[1]IMS Health, *Generic Drug Savings in the United States*, Generic Pharmaceutical Association, October, 2014.

in February 2016. However, four months later, my company still does not have product samples because the brand's staff won't export to our location. Without these samples, Amneal cannot begin developing a competitor, and patients are denied access, while the brand maintains monopolistic pricing power, despite the fact that all intellectual property and exclusivity protections have expired.

This refusal to provide samples may be direct, or take the form of the brand restricting the supplier from selling to generics or through unreasonable contract terms. In any case, it has nothing to do with safety – these samples are used solely for FDA-required testing, following FDA's review and approval of the competitor's safety protocols. Ultimately, the brand actions to keep generic firms from receiving samples makes it impossible for prospective competitors even to submit an application for FDA approval, thus indefinitely preventing patients from accessing affordable treatment options. These abuses undermine Hatch-Waxman. Simply put, no samples, no generics.

II. FEDERAL REGULATORS HAVE RECOGNIZED THESE ABUSES

These misuses have real costs: a 2014 study concluded the abuse of REMS and REMS-like limited distribution strategies cost the U.S. healthcare system $5.4 billion annually - $1.8 billion to the federal government[2]. But these abuses affect more than just payers – they have a direct impact on the costs borne by patients. A product to treat BP in lungs has averaged 13% yearly price increases since 2013[3], and has been embroiled in antitrust litigation. The Federal Trade Commission (FTC) has weighed in on similar cases noting, "a troubling phenomenon: the possibility that procedures intended to ensure the safe distribution of certain prescription drugs may be exploited by brand drug companies to

[2] Brill, Alex, Lost Prescription Drug Savings from Use of REMS Programs to Delay Generic Market Entry, Matrix Global Advisors, July, 2014.

[3] GPhA Anlayis of AWP data in Truven Health Analytics, Micromedex Solutions. RED BOOK Online. Bosentan. Oral. 62.5 mg. 30s ea.

thwart generic competition.[4]"

These abuses and the added costs they drive have not gone unnoticed by other federal regulators. In addition to the FTC's activity in this space, Dr. John Jenkins, M.D., the Director of the FDA's Office of New Drugs stated that, "the problem is the use of REMS blocking generic competition." He went on to say that "innovators have really become very aggressive in using that strategy [and] hiring the best lawyers to back up that strategy.[5]"

But access to samples is only part of the problem. The CREATES Act also addresses a common ploy by the brands to use the law's shared-REMS requirement to prevent launch of a filed and otherwise ready to be approved generic competitor. This involves the statutory requirement that, unless waived, the brand and follow-on products must enter into a single, shared safety protocol[6]. It has become another opportunity for brands to game the system.

A current example of this is Amneal's diligent efforts to join a REMS for a much-needed product in the critical effort to treat drug addiction. The brand's efforts to block generic access ended only after the FDA issued is first waiver of the single, shared-REMS requirement. It took more than three times longer than the 120 days in the current statute and your legislation. During the delay period, the brand made over a billion dollars, while payers – both public and private – paid full brand prices and patients did not have access to a more affordable generic. This delay is in spite of the fact that the REMS statute specifically prohibits its use to block or delay generics from coming to market[7].

---

[4] Brief for the Federal Trade Commission as Amici Curiae, Mylan Pharmaceuticals, Inc. v. Celgene Corporation, (No. 2:14-CV-2094-ES-MAH) Available: https://www.ftc.gov/policy/advocacy/amicus-briefs/2014/06/mylan-pharmaceuticals-inc-v-celgene-corporation

[5] Gingery, Derrick. REMS That Block Generics Are 'Major' Problem For FDA, Jenkins Says. "The Pink Sheet" Daily. January 8, 2015.

[6] Federal Food, Drug and Cosmetic Act § 505-1(i)(1)(B), 21 U.S.C. 355–1 (i)(1)(B)

[7] Federal Food, Drug and Cosmetic Act section 505-1(f)(8), 21 U.S.C. 355-1 (f)(8)

This also offers another example of a common tactic used by the brands, hiding behind claims of "protecting" patient safety and refusing to work with generic manufacturers who want to use equivalent protections for follow-on products. FDA has only limited authority to allow generic manufacturers to implement their own REMS programs, even when the agency has recognized the generic company's ability to satisfactorily implement the necessary precautions. We should be reminded that safety is the FDA's principle mission. Claims by the brand industry that a generic's safety protocols are somehow inadequate subtly undermine the Agency's record of success in ensuring the safety of the nation's drug supply.

Certain abuses of brand abuses keep important products off the market indefinitely, even after the FDA has determined that the company's follow-on product is just as safe and just as effective as the brand product, and even when the brand product's patent protection has expired. For example, a product to treat irritable bowel syndrome has averaged 12% price increases since 2008[8]. While a generic competitor entered the market last year, this occurred only after prolonged refusal by the brand to negotiate a shared-REMS, which FDA noted took more than three years, characterizing the brand's insistent delays as "pretextual appeals to safety as a means to delay that competition."[9]

Even once FDA provided a waiver for the generic manufacturers to operate an equivalent REMS program, the brand sued the agency in an attempt to force the generics back into the stalled negotiations. In the interim after the brand exclusivity expired and the FDA waiver, the

---

[8] GPhA Analysis of AWP Data from Truven Health Analytics, Micromedex Solutions. RED BOOK Online. Alosetron. Oral. 0.5 mg. 30s ea.

[9] Brief of Defendant Sylvia Matthews Burwell, et al. on Plaintiff's motion for a Temporary Restraining Order, Prometheus Laboratories, Inc. v. Sylvia Matthews Burwell, et al. (2015) (No. 1:15-CV-00742 (JEB)). Available at: http://www.fdalawblog.net/LOTRONEX%20-%20Roxane%20TRO-PI%20Opp.pdf

brand raised its price over 50%, much more rapidly than it had prior to the threat of generic competition[10].

III. REMS ABUSES ARE NOT NEW AND SHOW FEW SIGNS OF SLOWING

As the subcommittee knows, this is not a new problem. Almost five years ago the Senate passed legislation that included language – at FDA's request – to address it. In 2012, the Senate passed that language as part of the prescription drug user fee reauthorization[11]. Unfortunately the language fell out when the bill went to conference with the House of Representatives.

FDA has called for legislation to address related REMS abuse issues and Dr. Janet Woodcock, Director of the FDA's Center for Drug Evaluation and Research, addressed the point head-on in a January, 2016 Senate HELP Committee hearing. Specifically, she stated, "innovator companies feel it is their duty to their stockholders to delay completion as long as possible."[12]

The CREATES Act is well-crafted to ensure that FDA maintains its ability to oversee that generic manufacturers first have sufficient safety protocols in place to handle samples and second, can implement – when appropriate – equivalent REMS programs that offer comparable protections for patients without delaying approval for years with fruitless negotiations.

---

[10] GPhA Analysis of AWP Data from Truven Health Analytics, Micromedex Solutions. RED BOOK Online. Alosetron. Oral. 0.5 mg. 30s ea.

[11] Food and Drug Administration Safety and Innovation Act, S. 3187, 112th Congress (As passed by Senate May 24, 2012)

[12] *Generic Drug User Fee Amendments: Accelerating Patient Access to Generic Drugs. Before S. Comm. on Health, Education, Labor and Pensions*, 114th Congress (2016) (Comments by Janet Woodcock, MD, Director of Center for Drug Evaluation and Research at FDA). Available at: http://www.help.senate.gov/hearings/generic-drug-user-fee-amendments-accelerating-patient-access-to-generic-drugs

The potential for abuses is only growing. Nearly 40 percent of new FDA approvals are subject to REMS, and the percentage of REMS programs that require distribution restrictions referred to as Elements to Assure Safe Use (ETASU) has increased dramatically in the last several years. In 2009, roughly 75% of REMS programs only required medication guides – but now over 50% of REMS programs include limits on distribution.

As you know, many of your colleagues serving on various investigative committees have examined the growing use of self-imposed restricted distribution programs, but those investigations have tended to focus on high-profile examples, the practices they highlighted are by no means outliers. While Congress appears to be listening, statutory changes remain elusive. Many of the investigations have looked to the abuse of self-imposed restricted-distribution programs that are designed – often explicitly – to block generic entry.

For example, in an investor presentation, the pharmaceutical manufacturer Retrophin discussed how limiting distribution of the drugs Thiola® and Chenodal® to a single specialty pharmacy would block a lower-cost alternative from coming to market and serve to protect their product from competition[13]. Turing Pharmaceuticals also adopted the practice of using a closed distribution system as an effective block on generic competition. John Hass, the company's director of patient access, said so explicitly, noting that generics wishing to buy samples of the drug Daraprim® would not be welcome. Hass said:

> *"Most likely I would block [a generic purchase] …We spent a lot of money for this drug. We would like to do our best to avoid generic competition. It's inevitable. They seem to figure out a way [to*

[13] Retrophin: Manchester Pharmaceuticals Acquisition February 13, 2014. Available at: https://web.archive.org/web/20150226002409/http://www.retrophin.com/pdf/ManchesterAcquisitionAgreementConferenceCall.pdf

manufacture a generic alternative] no matter what. But I'm certainly not going to make it easier for them[14]*."*

These programs do not stand on any FDA safety requirements. Rather, the manufacturers choose to adopt REMS-like protocols because they know how effective a tool the program has been in blocking lower-cost alternatives from coming to market.

So while many opponents of REMS reform have argued that there are only a small number of products that are subject to REMS with ETASU, they ignore two very important facts. First, more and more products approved are subject to a REMS requirement, just setting the system up for further abuse. Second, there is no public record of what companies are already using restricted distribution networks to restrict access to specific drug samples, and FDA cannot prevent those contractual arrangements. Also, as the biosimilars market develops the high price of many new biologics will only incentivize further abuse of these types of arrangements, and create incredible excessive spending for the healthcare system through the loss of potential savings. The criticism that this is "too small" of a problem to look at is nothing more than attempt to create opportunity for further abuse.

IV. THE CREATES ACT IS A MEANINGFUL SOLUTION TO THE PROBLEM

The CREATES Act provides a narrowly-tailored — and desperately-needed — remedy to the many generics manufacturers that have been thwarted by these anti-competitive tactics. On one hand, it allows generic competitors to seek relief in court when brands refuse to provide product samples on commercially-reasonable, market-based terms. And on the other, it provides an essential remedy for generics companies

[14] Ed Silverman, *How Martin Shkreli prevents generic versions of his pricey pill*, Pharmalot, October 5, 2015. Available: http://pharmalot.com/how-martin-shkreli-prevents-generic-versions-of-his-pricey-pill/

when brands drag their feet during negotiations over a shared REMS program.

Importantly, the proposed legislation provides crucial safety protections for both patients and researchers by ensuring that the FDA both reviews and approves the follow-on applicant's testing protocols, informed consent documents, and informational materials before authorizing the follow-on applicant to obtain samples of brand-name products that are subject to an FDA-mandated REMS. I stress again that the FDA is the proper authority to review such documents, and claims by the brands that generics fail to provide them with proprietary clinical trial protocols is a red-herring. We trust that the Agency has the capacity to make suitable safety determinations, just as it did when the Agency approved the innovator's trial protocols and REMS. Finally, The CREATES Act specifically indemnifies brand manufacturers for any claim arising out of the failure of a generic manufacturer to follow adequate safeguards to assure safe use of the product.

Moreover, the manner in which the legislation is drafted appropriately limits any potential for frivolous litigation. The bill creates an affirmative defense for brands if they can show they are no longer manufacturing or restricting access to the product. To be clear, generic manufacturers have no interest in unnecessary litigation – our focus is simply that these samples should be available to us at a market price in order to achieve the patient access and competition goals of Hatch-Waxman. There would be no need for the court relief provided in the bill if brands do not actively impede this. It is our hope that having a clearer cause of action, as created here, will actually reduce the need to litigate over these matters.

I recognize that certain companies have announced their opposition to this legislation—just as they opposed the Hatch-Waxman Act in 1984, and just as they fought to prevent passage of the BPCIA in 2012. That opposition comes at a cost for consumers. Aside from critical restriction of patient access, I will again reference the Matrix Global Advisors estimate REMS abuse transfers some $5.4 billion per year from

consumers, private insurers, and public healthcare programs directly to their bottom line — while enabling them to continue raising prices long after their patent protection expires[15]. Clearly though, their gains are huge losses for patients in terms of both access and savings.

In conclusion: Even the most noble public policy initiatives, and the Hatch-Waxman Act and BPCIA qualify as noble achievements, require stewardship. The CREATES Act provides essential relief and remedies when brand companies refuse to provide samples on commercially reasonable terms or drag their feet during shared REMS negotiations. It will help make the promise of affordable medicine a reality for more Americans.

I urge prompt passage of the CREATES Act, and would be happy to address any questions the Subcommittee may have.

[15] Brill, Alex, Lost Prescription Drug Savings from Use of REMS Programs to Delay Generic Market Entry, Matrix Global Advisors, July, 2014.