Restricted Access Drug Program Abuses Impeding Patient Access to Generic Drugs
Myths and Facts Regarding REMS and the
Creating and Restoring Equal Access to Equivalent Samples ("CREATES") Act

Background – What are REMS and What is Current Law?

Under the Food and Drug Administration Amendments Act (FDAAA) of 2007, FDA can require manufacturers of drugs with known risks to develop a Risk Evaluation and Mitigation Strategies (REMS) program. REMS programs are designed to ensure that the benefits of a drug or biologic outweigh its risks to enable patients to have continued access to these medicines. The manufacturer of the drug develops the REMS program, which the FDA then reviews and approves. The specifics of the REMS program vary from drug to drug, which can include a Medication Guide, patient package insert, or communication plan. For certain drugs, the FDA can also require "Elements to Assure Safe Use" (ETASU) that include restricted distribution channels.
The Abbreviated New Drug Application (ANDA) for a generic and the 351(k) biologics license application (BLA) for a biosimilar of a brand drug with a REMS program must have the same or comparable ETASU. The statute also directs the brand manufacturer to negotiate with generic competitors to design and implement a single shared REMS program.

What is the Current Problem with REMS and Restricted Access Abuses?

Current law clearly states that a manufacturer cannot use a REMS program to block or delay approval of a generic drug application. However, certain brand companies continue to use REMS programs to delay competition by denying generic and biosimilars manufacturers access to samples of branded drug products, which are required to conduct the bioequivalence studies necessary for FDA approval. Without access to these samples, generic and biosimilars approvals are blocked and patients are left without access to more affordable medicines. Brand manufacturers have also used the requirement to institute a single, shared REMS plan to delay generic entry by prolonging these negotiations indefinitely. More recently, branded manufacturers have also begun applying restricted access programs to drugs for which the FDA has not required a REMS program in order to delay generic entry.

According to a July 2014 study conducted by Matrix Global Advisors, the ongoing abuse of REMS and REMS-like programs costs the U.S. health system $5.4 billion annually – $1.8 billion to the federal government.

Solution: The Creating and Restoring Equal Access to Equivalent Samples Act (CREATES) Act of 2017

The CREATES Act addresses the most common abuses of both REMS and non-REMS restricted access programs, while maintaining necessary safety protections for patient safety and public health.

Myths vs Facts

***Myth*:** REMS do not block generic competition – they are rare and ETASU are even rarer.

> **Fact:** Nearly 40 percent of new FDA approvals are subject to REMS, and the percentage of REMS programs that require distribution requirements has increased dramatically in the last several years. In addition, brand manufacturers have also begun imposing distribution restrictions on non-REMS products.
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> **Fact:** In 2009, roughly 75% of REMS programs only required medication guides – but now over 50% of REMS programs include elements to assure safe use. These safety requirements are appropriate and assure patient access to drugs that they otherwise would not be able to use. The problem is abuse of these safety requirements to delay generic competition.
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> **Fact:** The July 2014 study conducted by Matrix Global Advisors identified *40* drugs from just eight generic manufacturers where REMS and non-REMS restrictions are being used to block access. This ongoing abuse costs the U.S. health care system $5.4 billion annually.
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> **Fact:** FDA Office of New Drugs Director Dr. John Jenkins at a 2014 industry conference called the abuse a "growing major problem" for FDA. He went on to say, "I think companies have really gone to the extent of kind of abusing the system, because the system was designed to try to ensure the safe use of the drug and now it's become an evergreening system for avoiding generic competition." He added, "the problem is use of REMS to block generic competition and the innovators have really become very aggressive in using that strategy and hiring the best lawyers to back up that strategy.[1]" Dr. Janet Woodcock, M.D., director of FDA's Center for Drug Evaluation and Research has also weighed in on the issue, most recently testifying before Congress that these abuses are "a problem we struggle with a lot" and went on to note that they have "delayed [the] availability of generics."

***Myth*:** The proposal threatens patient safety involving medicines carrying serious risks and fails to ensure that generic manufacturers are capable of handling REMS drugs.

> **Fact:** Generic manufacturers are committed to patient safety. We support the REMS program when used as intended – to protect patients from severe side effects and adverse events and ensure they have access to these life-saving medicines. Generic and biosimilar companies have decades of experience in the testing and development of products with high safety profiles. Just because certain

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

drugs have REMS requirements does not mean that potential generic and biosimilars manufacturers should not have access to product samples.

Fact: The CREATES Act does not lower safety requirements, and instead ensures that only appropriate manufacturers receive these samples through an affirmative authorization from FDA that satisfies any relevant safety concerns, which they are required to produce publicly in court to make their claim.

Fact: The CREATES Act does not remove any existing authority that FDA has to ensure that generic manufacturers have taken necessary precautions to ensure patient safety. In fact the legislation only grants the FDA the authority to grant such authorization to the generic manufacturer when it has provided sufficient evidence to show that it can safely handle the product.

Fact: In instances where the brand manufacturer refuses to deal in good faith to develop a shared REMS, the bill simply gives FDA to take the same action it has already taken in other cases of abuse more expeditiously. FDA has already has the authority to decide that the burdens of a shared REMS, such as brand obstruction, can outweigh the benefits of a shared program and allow generics to develop a separate program. They have already done this in limited circumstances, and the CREATES Act would give them a clear opportunity for similar action in the future. All generic REMS programs are certified as equally sufficient in protecting patient safety, and solely exist due to the hurdles created by brand companies.

Fact: The CREATES Act would not move any authority that currently exists at FDA to the federal courts. It would simply give generic manufacturers the leverage necessary to get fair, market based access to samples necessary to meet FDA requirements.

***Myth*:** The proposal harms patient access to needed therapies by exacerbating drug shortages and directing products to generic companies instead of patients in need.

Fact: The CREATES Act does not require diversion of products away from patients, but only that the brand manufacturer not place restrictions on the sale of samples to generic manufacturers at commercially-reasonable, market-based terms. In fact, the legislation specifically exempts drugs that are in shortages. Moreover, ensuring that generic companies have appropriate access to samples for product testing could result in more manufacturers of a product and fewer drug shortages.

***Myth*:** FDA guidance will facilitate sale of REMS products for testing without "forced sale"

Fact: This is not a "forced sale". Inherent in the Hatch-Waxman statute, generic companies have access to product samples to conduct bioequivalence testing. This is about the abuse of safety requirements

by certain brand manufacturers to deny patients access to more affordable generic medications. In fact, the CREATES Act creates an affirmative defense for brand manufacturers who are acting in good faith.

Fact: While the guidance is a step in the right direction, there is no enforcement mechanism to ensure that brand companies provide samples to potential biosimilar and generic developers. As Dr. Jenkins noted at the same conference, "Congress gave us some tools to try to address generic entry but they are not as strong as they might have been to avoid what was probably an unexpected or unintended problem." The CREATES Act will help to address this issue in a market-oriented approach.

***Myth*:** The legislation unfairly shifts liability to brand manufacturers for claims that arise from circumstances and actions completely out of the innovators control.

Fact: 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.

***Myth*:** The legislation undermines important drug supply chain security improvements.

Fact: Nothing in the legislation amends or affects drug supply chain security legislation. In fact, the CREATES Act merely requires that the market function the same for generic manufacturers who seek to purchase samples as it would for any other legal purchaser.

***Myth*:** The proposal would allow generic manufacturers to infringe the intellectual property rights of brand manufacturers.

Fact: Nothing in the legislation affects a brand manufacturer's IP rights. Instead, the legislation merely maintains the balance established under the landmark Hatch-Waxman Act. Hatch-Waxman creates a specific litigation process for brands to make IP claims against generic manufacturers. The CREATES Act would not influence that litigation process at all. Additionally, patent law creates a specific, statutory exemption for any IP claims against the necessary efforts generic manufacturers must go through to get approval for a product. The samples being requested would be solely used for those protected purposes, and therefore would not infringe upon brand IP rights.

***Myth*:** The legislation is broader than necessary to address the supposed problem

Fact: The CREATES Act is a narrowly tailored proposal to address the well-documented problem of REMS abuses. It does not establish any new requirements on brand manufacturers. They merely must allow the marketplace to work as it should – without limiting the ability of generic manufacturers to purchase samples at commercially-reasonable, market-based prices. The bill establishes an affirmative defense for brand manufacturers in order to limit any potential frivolous litigation.

***Myth*:** The CREATES Act would expose the brand manufacturer to liability from the mishandling of their product after the sale from either the generic manufacturer or other third parties.

> **Fact:** The CREATES Act provides brand manufacturers with specific indemnity for any liability that would arise from the handling of the drug by the generic manufacturer. This indemnity would be above and beyond what brand manufacturers normally have when they provide products for generic testing for non-REMS products. Generic companies have the expertise, the regulatory oversight by FDA, and strong incentives to ensure the safe handling of brand product samples.

***Myth*:** The CREATES Act would create additional frivolous litigation that would clog up the court system.

> **Fact:** The CREATES Act would likely lessen the court system's case load related to REMS abuses. Brand manufacturers are already being sued over these practices through less clear statutory authorities. The CREATES Act would provide clarity, giving brand manufacturers a clear picture of the potential damages they face and create a very large incentive to handle these disputes privately between companies without any additional regulatory burdens or litigation costs.