

Drug Money Part 4 – The Return of the CREATES Act: Fourth Time's a Charm?

The [Creating and Restoring Equal Access to Equivalent Samples Act](#) (or CREATES Act) is the latest attempt by Congress to intervene to prevent anticompetitive behavior in the pharmaceutical industry. The intention of the CREATES Act is “to promote competition in the market for drugs and biological products by facilitating the timely entry of lower-cost generic and biosimilar versions of those drugs and biological products.”^[1] A [bipartisan group](#) of Senators introduced the most recent version of the CREATES Act into the current session of Congress on April 27, 2017, and Sen. Grassley (R-IA) [recently announced](#) that he wants to tie potential passage of the CREATES Act to the bill to renew funding for the Children’s Health Insurance Program (CHIP). The funding for CHIP [expired](#) on September 30 and Congress faces [intense pressure](#) to act soon. This is the [fourth time](#) Congress has introduced a similar bill,^[2] and many supporters from the health sector, including health insurers, providers, and patient organizations, [say the chances](#) have never been better. What does the CREATES Act do and why hasn’t it passed?

How Does the CREATES Act Change Current Laws?

The Food and Drug Administration Amendments Act (FDAAA)^[3] of 2007 gave the FDA the authority to request a Risk Evaluation and Mitigation Strategy (REMS) to ensure safer handling of medicines that have serious side effects or that are unusually subject to abuse. Currently, a drug subject to REMS requirements is typically sold directly from the manufacturer (not a distributor) to qualified medical professionals. Since the FDAAA does not require the manufacturer of brand-name drugs to sell to generic competitors, REMS restrictions give

brand manufacturers a way to deny generic manufacturers from getting samples. The [FDA requires](#) drug companies seeking approval for generic drugs to file an Abbreviated New Drug Approval (ANDA). When using an ANDA, manufacturers only need to provide evidence that their generic drug has a bioequivalent profile to the branded drug, enabling it to rely on the clinical trials performed for the branded drug to demonstrate safety and efficacy.[\[4\]](#) However, generic manufacturers need samples of the branded drug to demonstrate bioequivalence. Under current laws, if a branded drug company uses a restricted distribution system to deny competitors access to samples, it can delay or prevent the approval of competitive products at the FDA. Furthermore, unless a waiver has been granted, current law requires that a drug that is the subject of an ANDA, i.e., a generic equivalent, to share the same REMS with the branded equivalent.[\[5\]](#)

The CREATES Act requires license holders (brand manufacturers) to sell “sufficient quantities” of their drugs at “commercially reasonable, market-based terms” to product developers (generic manufacturers) to conduct testing required for an ANDA. If they fail to do so, a generic manufacturer can sue the brand manufacturer and “receive a monetary amount sufficient to deter the license holder from failing to provide other eligible product developers with sufficient quantities of a covered product on commercially reasonable, market-based terms.”[\[6\]](#) The courts will have to work out the details of what constitutes “commercially reasonable terms,” but a civil action in federal court for injunctive relief would be much easier to prove and enforce than a traditional private antitrust enforcement suit[\[7\]](#) – the only current remedy for product developers who are unable to purchase samples from license holders.

The CREATES Act reasonably exempts license holders who are experiencing a shortage in a product from the Act, unless the shortage lasts longer than 6 months. It also exempts companies

that no longer produce the drug, as long as neither the company nor any of its agents, wholesalers, or distributors are manufacturing the drug or have sufficient supplies in the inventory to sell to the generic manufacturer. The current version of the bill also includes a limitation of liability for brand manufacturers who sell the drug to a product developer who fails to maintain adequate safety standards (including disposal).

The CREATES Act also addresses the ability of license holders to refuse product developers from sharing a REMS that they have negotiated with the FDA for a specific product. Some companies have even patented their REMS and sued generic competitors that attempted to market a generic version of the drug.[\[8\]](#) The Act requires patent holders to negotiate the implementation of a shared REMS program with generic manufacturers,[\[9\]](#) and allows the Secretary of Health and Human Services (HHS) to implement a single, shared REMS program when the license holder and product developer are unable to reach an agreement.[\[10\]](#)

Importantly, the CREATES Act includes both traditional small molecule drugs and biologics.[\[11\]](#) The Act includes drugs approved under the Biologics Price Competition and Innovation Act of 2009,[\[12\]](#) which established an ANDA-like process at the FDA for biological products to demonstrate biosimilarity and interchangeability with a reference biological product.[\[13\]](#) In 2016, biologics accounted for approximately one-quarter of the pharmaceutical market and one-half of the FDA's approval of new chemical entities.[\[14\]](#) As a result of the increasing importance of biological drugs, the CREATES Act inclusion of biologics is critical.

Is This Bill Really Necessary?

In 2015, Turing Pharmaceuticals made national headlines by raising the price of Daraprim, a drug that treats rare toxoplasmosis and cystoisosporiasis infections, from \$13.50 to

\$750 per pill.^[15] Martin Shkreli, the former CEO of Turing, [implemented](#) a controlled distribution system for Daraprim, maintained a list of qualified buyers, and forced all individual prescriptions to be filled by the specialty pharmacy unit at Walgreens.^[16] As a result, the company could refuse sales to any generic manufacturers. Since Turing established a monopoly and kept all competition out of the market, it was able to increase the cost of the drug by 5500% overnight.

While the actions of Shkreli and Turing may be particularly egregious, they are not unique. As of March 2016, the FDA had received approximately 150 inquiries from generic manufacturers about their inability to secure sufficient samples.^[17] A 2014 study by the Generic Pharmaceutical Association (GPhA) found that nearly 40% of new FDA approvals contained REMS-based restrictions and that manufacturers were imposing distribution restrictions even when they were not required by the FDA.^[18] The study by the GPhA calculated that misuse of REMS to delay market-entry of generic competition for forty brand name drugs costs the health care system \$5.4 billion annually.^[19] The Congressional Budget Office [estimates](#) that the CREATES Act could save \$3.3 billion in federal spending over ten years with additional savings to individuals and private insurers that could be much greater.

Robin Feldman, Professor of Law and Director of the Institute for Innovation Law at the University of California, Hastings College of the Law, [testified](#) before a Senate Subcommittee that “an important safety program is being hijacked to block competition...The CREATES Act does an admirable job of assigning the right jobs to the right branches of government.” As Mytheos Holt [reported](#) in the American Spectator, “big pharmaceutical companies abuse safety measures... as a means to keep control of the market for drugs that have already lost patent protections. It’s basic anticompetitive behavior, and it’s technically already illegal, but the means to remedy it

is often too expensive and time consuming for many companies to engage in. The CREATES Act reforms that.”[\[20\]](#)

So Why Hasn’t It Passed Already?

Simply put, Big Pharma has spent [millions](#) to oppose the CREATES Act. Big Pharma [argues](#) that patients could be harmed by product developers who enter into clinical trials without proper safety protocols.[\[21\]](#) Proponents of the bill [counter](#) that the FDA is still responsible for approving clinical trials of any generic competitor and the CREATES Act does nothing to weaken that oversight.

Opponents of the bill also invoke fundamental rights of intellectual patent holders. Erika Lietzan, Associate Professor of Law at the University of Missouri, asserts that the CREATES Act would “require the company to practice its patent for the benefit of its competitor, even though it is a bedrock principle of U.S. patent law that a patent owner has no duty to practice its patent at all.”[\[22\]](#) Lietzan argues that license holders would need to manufacture essentially unlimited quantities of the drug for its competitors to enable them to complete the clinical trials required to obtain FDA approval. For biological products, approval of a biosimilar could require clinical trials of hundreds of patients lasting for a year or longer,[\[23\]](#) so the number of samples required could be substantial. This criticism is ideological, however. The CREATES Act specifically exempts companies from having to practice their patent if they no longer manufacture the drug or have samples in the inventory. In addition, brand manufacturers can profit from the sale of product to developers because product developers need to provide commercially reasonable compensation for the samples.

Lietzan also argues that the FDA already has the authority to approve ANDAs if applicants are unable to acquire samples for testing, although the FDA has not exercised this authority except to allow some companies to access samples from foreign

affiliates when no U.S.-based distributor had the drug.[\[24\]](#) The CREATES Act does not change any of the FDA's authority, so the FDA would continue to have this theoretical authority. In addition, the CREATES Act would increase the amount of information the FDA has when making an ANDA approval decision because product developers could test for bioequivalency.

While Lietzan is correct that the U.S. does not compel the manufacture of goods for sale, her argument fails to acknowledge that pharmaceuticals have additional regulatory barriers to entry in addition to patent protections, and that competitors face significant barriers to market entry that require them to purchase a current product for testing. The Federal Trade Commission (FTC) expressed concern that the REMS program, designed to "ensure the safe distribution of certain prescription drugs[,] may be exploited by brand drug companies to thwart generic competition."[\[25\]](#) The FTC cites the "unique regulatory framework that applies to the pharmaceutical industry," specifically that the FDA requires bioequivalence testing for marketing approval and notes that Congress included language in the FDAAA of 2007 to say that REMS should not be used to block or delay approval of an ANDA.[\[26\]](#) The CREATES Act simply codifies Congress's intentions when it established the REMS program by creating a more direct and less expensive path for generic manufacturers to legally obtain the needed samples if brand manufacturers refuse to sell samples to them. The CREATES Act grants product developers the ability to bring an action in federal court to force brand-name manufacturers to provide samples in a much cheaper, easier, and more predictable process than traditional antitrust litigation. The threat of large financial penalties should encourage license holders to sell samples to competitors and help keep these kinds of anticompetitive lawsuits out of the court system.

Conclusion

More than 37 signatories including AARP, the American College

of Physicians, and the American Hospital Association have called on Congress to pass the CREATES Act.^[27] Nearly three-quarters of the American public [believe](#) that reducing prescription drugs costs should be the top public health care priority for the President and Congress. President Trump [repeatedly commented](#) that prescription drugs were too costly and that drug companies were “frankly getting away with murder.” Bipartisan support for the CREATES Act suggests that the time is ripe for legislative action to prevent anticompetitive behavior by pharmaceutical companies. The CREATES Act is a small, but meaningful step toward ensuring that drug companies cannot use creative legal strategies and regulatory programs intended to protect patients to increase profits.

[\[1\]](#) The Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2017, S. 974 and H.R. 2212 (115th Congress).

<https://www.congress.gov/bill/115th-congress/senate-bill/974/text>.

[\[2\]](#) The Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2016, S.3056 (114th Congress) did not pass. Previous attempts were made in H.R. 2900 (110th Congress) and S. 3187 (112th Congress). The Senate Bill passed the Senate May 24, 2012, but the House did not. Similar bills, including the FAST Generics Acts of 2014 and 2015 H.R. 2841 (114th Cong.) and H.R. 5657 (113th Cong.), contained provisions aimed at preventing patent holders from using REMS to delay market entry of competitors.

[\[3\]](#) 21 U.S.C.A. § 355-1 (2017).

[4] 21 CFR § 314.94(a)(7) (2017); The proposed generic must have the same active ingredient, route of administration, dosage form, and strength, 21 U.S.C. § 355(j)(2)(A)(iii).

[5] Federal Food, Drug, and Cosmetic Act (FD&C Act) § 505-1(i)(1)(B). Specifically, any drug approved via an ANDA must share a single system of elements to assure safe use (ETASU) with its branded equivalent ([21 U.S.C. 355-1](#)).

[6] CREATES Act § 3(b)(4)(A)(iii). The monetary amount is capped at the revenue the license holder earned on the covered product during the time the developer was unable to access the product (§ 4(B)(i)(II)).

[7] Brennan, Zachary. "House and Senate Revive Bill Targeting Generic Drug Delays." *Regulatory Affairs Professionals Society*. Published April 27, 2017. Available at: <http://raps.org/Regulatory-Focus/News/2017/04/27/27430/House-and-Senate-Revive-Bill-Targeting-Generic-Drug-Delays/#sthash.i0rlj002.dpuf>.

[8] Sarpatwari A, Avorn J, Kesselheim AS. Using a drug-safety tool to prevent competition. *N Engl J Med*. 2014;370(16):1476-1478. This article cites the case of Celgene, which patented its REMS for thalidomide (Thalomid) and then sued Barr Laboratories when they tried to market a generic version of the drug and use the same REMS.

[9] Statement of Senator Patrick Leahy On Introduction of the Creating and Restoring Equal Access to Equivalent Samples (CREATES) (June 14, 2016). Available at: <https://www.leahy.senate.gov/press/statement-of-senator-patrick-leahy-on-introduction-of-the-creating-and-restoring-equal-access-to-equivalent-samples-creates>.

[10] CREATES Act §4(2)(B)(ii).

[11] Robin Feldman, Hearing on the CREATES Act: Ending Regulatory Abuse, Protecting Consumers and Ensuring Drug Price

Competition, Senate Committee on the Judiciary, Subcommittee on Antitrust, Competition Policy, and Consumer Rights (June 21, 2016). Available at <http://www.uchastings.edu/news/articles/2016/06/creates-act-feldman-testimony.php> and <https://www.judiciary.senate.gov/imo/media/doc/06-21-16%20Feldman%20Testimony.pdf>; Feldman, Robin, and Evan Frondorf. "Drug Wars: A New Generation of Generic Pharmaceutical Delay." *Harvard Journal on Legislation* 53 (2016).

[12] Subtitle A of title VII of [Public Law 111-148](#); 124 Stat. 804

[13] [42 U.S.C. 262\(k\)](#) section 351(k).

[14] Denis Kent, Sarah Rickwood, and Stefano Di Biase. "Disruption and maturity: The next phase of biologics. Quintiles IMS Health White Paper. http://www.imshealth.com/files/web/Global/white%20paper/QI_Disruption_and_maturity_The_next_phase_of_biologics.pdf.

[15] Pollack A. "Drug Goes From \$13.50 a Tablet to \$750, Overnight." *The New York Times*. Published September 20, 2015. https://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html?_r=0.

[16] <http://pharmalot.com/how-martin-shkreli-prevents-generic-versions-of-his-pricey-pill/>

[17] Kerstin Noëlle Vokinger, Aaron S. Kesselheim, Jerry Avorn, "Strategies That Delay Market Entry of Generic Drugs" *JAMA Intern Med*. Published online September 18, 2017. doi:10.1001/jamainternmed.2017.4650.

[18] Brill, Alex "Lost Prescription Drug Savings from Use of REMS Programs to Delay Generic Market Entry." *Matrix Global Advisors*. July 2014. Available at: http://www.gphaonline.org/media/cms/REMS_Studyfinal_July2014.p

[df.](#)

[19] *Ibid.*

[20] Holt, Mytheos. "The CREATES Act is Back" *The American Spectator*. April 28, 2017. Available at: <https://spectator.org/the-creates-act-is-back/>

[21] Pharma also argues that brand manufacturers could be liable if a product is not handled properly by a product developer, but this concern should be minimized by the most recent version of the CREATES Act (S. 974 and H.R. 2212 – 115th Congress).

[22] Erika Lietzan "A Second Look at the CREATES Act: What's Not Being Said" 17 *The Federalist Society Review* Issue 3, Forthcoming. Available at: <http://ssrn.com/abstract=2845041>.

[23] <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm291128.pdf>

[24] *Ibid.*

[25] Brief for *Actelion Pharmaceuticals v. Apotex Inc.*, Federal Trade Commission as Amicus Curiae. Case No. 1:12-cv-05743-NLH-AMD. Filed March 11, 2013. Available at: https://www.ftc.gov/sites/default/files/documents/amicus_briefs/actelion-pharmaceuticals-ltd.et-al.v.apotex-inc./130311actelionamicusbrief.pdf.

[26] 21 U.S.C. § 355-1(f)(8).

[27] <http://www.csrxp.org/37-signatories-call-on-congress-to-pass-creates-act/>