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Committee on the Judiciary  
Subcommittee on Regulatory Reform,  
Commercial and Antitrust Law**

**Hearing on Antitrust Abuses and the  
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\* The title and affiliation are for identification purposes. The views expressed here are my own, and do not reflect the views of Boston College or any other organization.

## **I. Patents And Generic Competition Give Us Important Balance Between Innovation and Distribution of Drugs**

The United States has an incredibly successful ecosystem for drug innovation and distribution. Patent protection for innovative medicines, combined with competition from generics when patents expire, have given us many life-saving advances, that become vastly less expensive when the patents expire and generic competitors enter the market. The 1984 Hatch Waxman Act<sup>1</sup> and the Biologics Price Competition and Innovation Act of 2009 (“BPCIA Act”)<sup>2</sup> have worked very well, for the most part, to encourage generic entry to the market once drug patents expire. The result has been a system that gives strong encouragement for researching and developing new drugs, as well as encouragement of generic versions entering the market and driving prices down as soon as drug patents expire.

This dual approach of encouraging innovation through the grant of twenty-year patent monopolies, and encouraging generic competition through the incentive mechanisms of Hatch Waxman and the BPCIA Act has worked well and is the approach that we should continue to follow. There has been no fundamental change to the market conditions for drug development and distribution that require a new approach. Nonetheless, problems with excessive price spikes for drugs and prevention of generic competition have arisen. These problems are not market failure problems, however. Rather, these problems are regulatory abuse problems, and the best solution is to fix the regulations that are being abused. The CREATES Act is narrowly tailored to do just that.

## **II. Abuse of Closed Distribution a Real Problem that CREATES Act Is Narrowly Tailored to Fix**

The FDA, as part of its authority to approve or remove drugs for sale, has required safety measures, including restricted distribution systems for certain dangerous drugs. The Food and Drug Administration Amendments Act of 2007<sup>3</sup> (“FDAAA”) formalized the FDA’s authority to place restrictions on dangerous drugs. The FDAAA created an important new tool for dealing with drugs that have potential safety problems by authorizing the FDA to require drug sponsors to submit a safety plan, called a Risk Evaluation and Mitigation Strategy (“REMS”), to ensure that the benefits of certain prescription drugs outweighed their risks.<sup>4</sup>

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<sup>1</sup> Drug Price Competition and Patent Term Restoration Act, P.L. 98-417, 98 Stat. 1585 (1984).

<sup>2</sup> Sections 701-703 of the Patient Protection and Affordable Care Act, P.L. 111-148, 124 Stat. 119 (2010).

<sup>3</sup> PUBLIC LAW 110-85—SEPT. 27, 2007 121 STAT. 823, available at <https://www.gpo.gov/fdsys/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf>.

<sup>4</sup> 21 U.S.C. § 355-1.

## FDAAA and REMS

The FDA has provided a brief overview of REMS basics<sup>5</sup> based on the FDAAA.<sup>6</sup> REMS are required risk management plans that use risk minimization strategies beyond the professional labeling to ensure that the benefits of certain prescription drugs outweigh their risks.<sup>7</sup> Examples include patient education of initial warning signs of infections prior to prescribing, liver function monitoring while a patient is taking a drug, and negative pregnancy test prior to dispensing of each prescription. FDA can require REMS if the agency determines that safety measures are needed beyond the professional labeling to ensure that a drug's benefits outweigh its risks. Drug sponsors develop REMS programs, and FDA reviews and approves them. FDA can require a REMS before or after a drug is approved. REMS can be required for a single drug or a class of drugs. Healthcare professionals and distributors may need to follow specific safety procedures prior to prescribing, shipping, or dispensing the drug. Each REMS has specific safety measures unique to the safety risks associated with a particular drug or class of drugs. That is, no two REMS are exactly alike.

A REMS system may include one or more of the following elements: (1) a medication guide or patient package insert written in non-technical language; (2) a communication plan which educates, informs and raises awareness of risk; (3) Elements to assure safe use (ETASU) requirements intended to reduce a specific serious risk listed in the labeling of the drug; and (4) an implementation system to monitor and evaluate those in the healthcare system who are responsible for implementing ETASU measures. Additionally, all REMS systems are required to have a timetable for planned assessments of the REMS system after 18 months, 3 years, and in year 7 post-approval.<sup>8</sup> These assessments should include an evaluation of whether the REMS elements are meeting the REMS objectives and goals, and also whether the REMS elements, objectives, or goals need amending. Finally, these assessments may result in the elimination of a REMS system, if it has been determined that the REMS system has met its goals.<sup>9</sup>

The FDA maintains a database of approved REMS programs.<sup>10</sup> Presently, there are 71 individual and shared system REMS, including 42 which include ETASU requirements.<sup>11</sup>

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<sup>5</sup> FDA Basics Webinar: A Brief Overview of Risk Evaluation and Mitigation Strategies (REMS), available at

<https://www.fda.gov/AboutFDA/Transparency/Basics/ucm325201.htm>.

<sup>6</sup> *Id.*

<sup>7</sup> *Id.*

<sup>8</sup> Susan C. Nicholson, Janet Peterson, and Behin Yektashenas, *Risk Evaluation and Mitigation Strategies (REMS). Educating the Prescriber*. 35 Drug Saf. 2, 91-104 (2012).

<sup>9</sup> FDA Basics, *supra*, note 5.

<sup>10</sup> Approved Risk Evaluation and Mitigation Strategies (REMS), available at <https://www.accessdata.fda.gov/scripts/cder/remis/index.cfm>.

<sup>11</sup> *Id.*

## REMS with ETASU

ETASU (elements to assure safe use) are required medical interventions or other actions healthcare professionals need to execute prior to prescribing or dispensing the drug to the patient.<sup>12</sup> Some actions may also be required in order for the patient to continue on treatment. Depending on the risk, a REMS may require any or all of the following: (1) Prescribers have specific training/experience or special certifications (may be required to demonstrate ability to diagnose or monitor); (2) Pharmacies, practitioners or healthcare settings that dispense the drug be specially certified (agree to fill only after checking a lab value); (3) Drug be dispensed only in certain healthcare settings (e.g., infusion settings, hospitals, staff specifically trained); (4) Drug be dispensed with evidence of safe use conditions such as laboratory test results (liver enzyme or pregnancy test); (5) Each patient using the drug be subject to monitoring (follow up visit, still an appropriate patient); and (6) Each patient using the drug be enrolled in a registry. It should be noted that some drugs would not be approved, or would be removed from the market, but for a REMS with ETASU to ensure that the drug benefits outweigh their risks.<sup>13</sup>

Celgene's thalidomide (Thalomid) provides an example of an extensive ETASU, due to the serious risks of embryo-fetal exposure to the drug product.<sup>14</sup> The REMS with ETASU for Thalomid requires that all prescribing healthcare providers are specifically certified, that all patients are informed of the risks of use and exposure to unborn children, that all patients are enrolled in a special program, and that all patients are actively monitored, particularly for instances of pregnancy.<sup>15</sup> In addition, the REMS with ETASU establishes a restricted distribution program for Thalomid. This restricted distribution program was developed by Celgene and is the subject of patent protection.

### ETASU Not to Be Used to Deny Access to Samples; ETASU to Be Shared

The FDAAA specifically mandates that no REMS with ETASU may be used to block or delay approval of a generic Abbreviated New Drug Application.<sup>16</sup> The Act also requires that for any brand drugs subject to REMS or REMS with ETASU programs, the brand company must share its REMS with ETASU with any approved generics.<sup>17</sup> Alternatively, the Act provides that the Secretary may waive the

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<sup>12</sup> FDA Basics, *supra*, note 5.

<sup>13</sup> *Id.*

<sup>14</sup> For the full story of Celgene's use of REMS with Thalomid, see Jordan Paradise, *REMS as a Competitive Tactic: Is Big Pharma Hijacking Drug Access and Patient Safety?*, 15 *Houston J. of Health Law and Pol'y* 43, 43-82 (2015).

<sup>15</sup> Thalomid (thalidomide) REMS, NDA # 020785 (Initial REMS Approved Aug. 2010; Most Recent Modification April 2016), *available at* [https://www.accessdata.fda.gov/drugsatfda\\_docs/remis/Thalomid\\_2016-04-22\\_Full.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/remis/Thalomid_2016-04-22_Full.pdf).

<sup>16</sup> 21 U.S.C. § 355-1(f)(8) (specifying that no REMS "element to assure safe use" of an established drug may be used to "block or delay approval of" a generic drug application).

<sup>17</sup> For simplicity, I use the terms "brand drugs" and "brand companies" to refer to registered listed drugs and the owners of listed drugs, respectively. I use the terms "generics" and "biosimilars" to refer to entities seeking to produce generics of small molecule and large molecule biologics, respectively, except that sometimes I use "generics" to refer to generic small molecule drugs and large molecule biosimilars collectively.

requirement to use a single, shared ETASU and allow a generic to use a different, comparable ETASU if (a) the burden of using a single, shared ETASU outweighs the benefit, or (b) the ETASU is protected by a patent or trade secret claim, and the generic has been unable to negotiate a license to the ETASU from the brand company.<sup>18</sup>

### **Using REMS or Restricted Distribution to Deny Access to Samples**

There are reports of numerous generics being unable to acquire samples of brand drugs for their ANDA applications.<sup>19</sup> A number of brand drug companies with drugs covered by REMS programs have refused to share their drugs with generics, citing REMS as the reason not to share.<sup>20</sup> Other companies have adopted restricted distribution systems without any requirement from the FDA to do so, and have used the restricted distribution systems to deny access to samples to generics.<sup>21</sup>

The FDA has sought to encourage and assure brand companies that they may—and should—share samples of listed drugs with generics for purposes of testing for ANDA applications.<sup>22</sup> The FDA has reviewed the safety protocols for individual bioequivalence studies, and has issued letters to brand companies stating that sharing samples with the generic for purposes of bioequivalence testing is not a violation of the listed drug’s REMS ETASU program.<sup>23</sup> The FDA has also issued guidance describing how to obtain such a letter, and reiterating that sharing samples with generics whose studies have been certified by the FDA does not violate any REMS. Nevertheless, brand companies continue to argue that they are justified in not sharing samples with generics because it could be a violation of their

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<sup>18</sup> 21 U.S.C. § 355-1(i)(1)(b).

<sup>19</sup> See Testimony of Dr. Janet Woodcock, “Generic Drug User Fee Amendments: Accelerating Patient Access to Generic Drugs” January 28, 2016 HELP Hearing, Trans. at 51:4–14, available at <https://www.help.senate.gov/hearings/generic-drug-user-fee-amendments-accelerating-patient-access-to-generic-drugs>:

[T]he companies on their own behalf have restricted programs that we do not really understand, but they are not related to REMS. We have had over 100 inquiries from generic companies who cannot get a hold of the innovator drug to compare their drug to. We have done everything we can to—we have written a letter saying, you know, that REMS does not require this, you can give it out for this purpose, and so forth, and we also refer these to [the Federal Trade Commission], okay? But we still continue to get complaints from generic companies that they cannot get a hold of the drug to make the comparison they need to do.

<sup>20</sup> See Statement Of Beth Zelnick Kaufman Before The Senate Judiciary Subcommittee On Antitrust, Competition, Policy And Consumer Rights, at 2-3 (June 21, 2016), available at <https://www.judiciary.senate.gov/imo/media/doc/06-21-16%20Zelnick-Kaufman%20Testimony.pdf>.

<sup>21</sup> See *id.*, at 7-8; Testimony of Dr. Janet Woodcock, *supra*, note 19.

<sup>22</sup> *Id.*

<sup>23</sup> See U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research, *How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD Guidance for Industry* (December 2014), available at <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm425662.pdf>.

REMS ETASU programs.<sup>24</sup> In addition, notwithstanding the plain language of the FDAAA that REMS ETASU may not be used to block or delay approval of a generic drug, some argue that brand companies have no obligation to share samples with generics whatsoever, nor should they.<sup>25</sup>

Finally, some brand companies have put drugs that do not present safety risks sufficient to require REMS into restricted distribution systems. This tactic has been used—particularly for drugs whose patents have expired—as a way to prevent generics from obtaining access to samples of the drugs for ANDA filings.<sup>26</sup>

Thus far, the majority of brand companies have not used restricted distribution systems or REMS with ETASU as a basis to deny samples to generics. But the use of this tactic seems to be growing.<sup>27</sup> More troublingly, if the tactic proves successful, the pressure for all drug companies to use it will increase. In fact, it may come to be seen as incompetent not to take steps to forestall generic competition by putting a drug into restricted distribution and refusing to share it. It is well known that brand companies spend significant money and efforts to extend their drug monopolies.<sup>28</sup> There is no reason that restricting samples will not be an increasingly attractive tool in this toolbox.

The situation for biologics is even more dire. Because of the nature of large-molecule biologic therapeutics, and because the biologic can change some over time, testing biologics for bioequivalence is a much more difficult and cumbersome task, that generally involves clinical trials. Thus the number of samples for testing biologics is much higher. In addition, these samples may be needed repeatedly, over the course of a year or more. If a brand company refuses to share samples in the middle of a biosimilar's testing, the entire testing process could be ruined, and the generic biosimilar maker may have to start over. If a brand company is able to employ this tactic regularly, the incentive to attempt to get biosimilar approval could be greatly reduced. Thus, it is crucial that biosimilars have timely access to numerous samples when needed as part of their testing processes.

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<sup>24</sup> See Written Testimony of Peter Safir, Senate Committee on the Judiciary Subcommittee on Antitrust, Competition Policy and Consumer Rights Hearing on the CREATES Act of 2016 (S. 3056), at 6 (June 21, 2016), available at <https://www.judiciary.senate.gov/imo/media/doc/06-21-16%20Safir%20Testimony.pdf>.

<sup>25</sup> See, e.g., Erika Lietzan, *A Second Look at the CREATES Act: What's Not Being Said*, 17 FEDERALIST SOC'Y REV. 3 (2016), available at [http://www.fed-soc.org/publications/detail/a-second-look-at-the-creates-act-whats-not-being-said#\\_ftnref97](http://www.fed-soc.org/publications/detail/a-second-look-at-the-creates-act-whats-not-being-said#_ftnref97) (arguing that patent owners may refuse to sell to generics based on the "bedrock principle of U.S. patent law that a patent owner has no duty to practice its patent at all.").

<sup>26</sup> Ed Silverman, *How Martin Shkreli prevents generic versions of his pricey pill*, Stat Pharmalot (Oct 5, 2015), available at <http://pharmalot.com/how-martin-shkreli-prevents-generic-versions-of-his-pricey-pill/> (quoting Jon Haas, Director of Patient Access at Turing Pharmaceuticals:

Most likely I would block that 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 make generics], no matter what. But I'm certainly not going to make it easier for them. We're spending millions and millions in research to find a better Daraprim, if you will.

<sup>27</sup> See Statement of Beth Zelnick Kaufman, *supra*, note 20.

<sup>28</sup> Shuchi Midha, *Strategies For Drug Patent Ever-Greening In The Pharmaceutical Industry*, 3 INT'L J. OF PHARM. SCI. AND BUS. MANAGEMENT, 11-24 (March 2015).

### **CREATES Act Is Narrowly Tailored Solution to Failure to Share Samples**

The CREATES Act is a narrowly tailored solution to the problem of some brand companies refusing to share samples with generics for ANDA applications. The Act creates a civil cause of action against a brand company that refuses to share sufficient samples for ANDA or Biosimilar applications. Specifically, the Act requires that brand companies sell samples on “commercially reasonable, market based-terms” within 31 days of a request by a generic. If the drug is covered by REMS with ETASU, then the brand company must sell to the generic within 31 days of receipt of an authorization to sell to the generic from the Secretary of Health and Human Services (“HHS”). Such an authorization is given after the Secretary reviews the generic’s protocols and sets any conditions for testing.

The brand company is not required to sell to the generic if the listed drug is available through others such as wholesalers, so long as the brand company does not restrict its wholesalers from selling to generics. Likewise, if there is a short-term (less than six months) shortage of the listed drug, the brand company is not required to sell to the generic. For a long-term shortage, the brand company must sell samples. This makes sense, because the solution to a long-term shortage could be more companies producing the drug.

The remedies available for the failure of a brand company to share are:

- (a) an injunction ordering the brand company to sell samples at commercially reasonable rates;
- (b) reasonable attorneys’ fees; and
- (c) a monetary award to deter such behavior, up to the revenue for the listed drug during the time that the brand refused to sell.

Importantly, the CREATES Act also formally removes liability from the brand companies for sharing with generics in accordance with the system set up by the Act. Thus the CREATES Act removes this concern, which some brand companies have cited in refusing to sell to generics.

### **III. The CREATES Act Also Remedies Refusal to Share REMS with ETASU**

#### **Sharing REMS with ETASU**

In addition to performing bioequivalence studies to support an ANDA, generic manufacturers must also comply with any drug related REMS, according to the FDAAA.<sup>29</sup> The FDAAA requires that generic and brand manufacturers “use a single, shared system” for risk mitigation unless the brand manufacturer’s system is too burdensome or is protected by a patent or trade secret that the brand company will not license:

355-1(i)(1)(B) . . . A drug that is the subject of an [ANDA] and the listed drug shall use a single, shared [ETASU] system under subsection (f). The Secretary may waive the requirement . . . and permit the applicant to use a different [ETASU], if—

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<sup>29</sup> See 21 U.S.C. § 355-1.

(i) the burden of creating a single, shared system outweighs the benefit of a single system . . . ; or

(ii) an aspect of the [ETASU] . . . is claimed by a patent that has not expired or is a method or process that, as a trade secret, is entitled to protection, and the applicant for the [ANDA] certifies that it has sought a license . . . and that it was unable to obtain a license.<sup>30</sup>

In the event that the generic manufacturer is unable to use a single, shared system, FDA has provided guidance for how to obtain a letter from FDA stating that their bioequivalence study protocols contain safety protections comparable to applicable REMS for the listed drug.<sup>31</sup> As discussed above, the guidance also states that FDA will not consider it a violation of the REMS for the brand company to provide a sufficient quantity of the listed drug to the interested generic firm or its agent to allow the firm to perform the testing necessary to support its ANDA.

### REMS Patents

The FDAAA contains language that implicitly authorizes companies to obtain patents on their REMS systems.<sup>32</sup> A number of brand companies have received patents on their REMS with ETASU. Five examples are: Entereg (Cubist Pharmaceuticals, now Merck); Pomalyst (Celgene Corporation); Revlimid (Celgene Corporation); Thalomid (Celgene Corporation); Xyrem (Jazz Pharmaceuticals, Inc.).<sup>33</sup> Of these five products, four (Revlimid, Thalomid, Xyrem, and Pomalyst) have been subject to ANDA filings.<sup>34</sup> Each of these five products has their REMS patents listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book).<sup>35</sup>

Because the requirements for REMS with ETASU are very specific, and individual ETASU are negotiated with the FDA, there is not a lot of room for creativity when it comes to creating ETASU. Indeed, the creation of an ETASU is governed very much by statute, with exact details supplied by necessity to assure safe use of the specific drug at issue. The FDAAA sets out specific steps that may be required for an ETASU, including:

(A) only allowing doctors to prescribe if they have been educated about the drug and certified,

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<sup>30</sup> *Id.*

<sup>31</sup> U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research, *How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD Guidance for Industry* (December 2014), available at <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm425662.pdf>.

<sup>32</sup> 21 U.S.C. § 355-1(i)(1)(B)(ii) (allowing the Secretary to waive requirement of single, shared REMS with ETASU if “an aspect of the elements to assure safe use for the applicable listed drug is claimed by a patent”).

<sup>33</sup> Ameet Sarpatwari, Jerry Avorn, and Aaron S. Kesselheim, *Using a Drug-Safety Tool to Prevent Competition*, 370 N. ENGL. J. MED. 1476, 1476-78 (2014).

<sup>34</sup> See *id.*; Celgene, *Celgene Notified of ANDA Filing for Pomalyst* (April 3, 2017), available at <http://ir.celgene.com/releasedetail.cfm?releaseid=1019949>.

<sup>35</sup> Sarpatwari, et. al, *supra*, note 33.

- (B) only allowing certain pharmacies, practitioners, or health care entities that are specially certified to distribute the drug,
- (C) only dispensing the drug in certain settings, such as certified hospitals
- (D) requiring patient testing (including follow ups if needed) to screen for risk,
- (E) counseling patients about risks and use,
- (F) monitoring (testing) each patient to maintain safe use conditions
- (G) maintaining a database of relevant information about patients, doctors and pharmacies.<sup>36</sup>

A look at the REMS patents filed by brand companies show that they track closely to the ETASU requirements set out in the FDAAA. For example, Claim 1 from Merck's REMS Patent for Entereg, reads as follows:

1. A method for delivering a drug to hospital patients . . . wherein the drug requires compliance with [REMS] [comprising]:
  - identifying [relevant] hospitals
  - providing said . . . hospitals with literature . . . ;
  - wherein the drug is [Entereg or generic] . . . ;
  - identifying subpopulation hospitals which have measures in place to limit use of drug . . . ;
  - wherein said measures comprise order sets, protocols or guidelines, residing on an integrated information system . . . ;
  - registering said subpopulation in a computer readable storage medium;
  - authorizing said subpopulation to receive shipment of the drug; and
  - dispensing the drug to the patients in said subpopulation for short-term use;
  - wherein the patients are hospital inpatients and the delivery is limited to in-hospital; and
  - monitoring the patients for said observed adverse event.<sup>37</sup>

In comparing Merck's Entereg ETASU patent to the requirements of the statute, one sees that there is little difference between the statutory requirements and the patent, other than the patent specifying that it is for use with Entereg or equivalents. Thus, questions of validity of the patent are immediately raised, such as obviousness. Nevertheless, the fact that Merck has a patent on its ETASU is a powerful tool to use against generics seeking to distribute the drug. If Merck does not choose to license its ETASU patent to generics and share its REMS with ETASU with the generic (which the FDAAA does not require it to do), then the generic's only other option is to seek allowance from the Secretary to develop a comparable ETASU. But can a generic develop a comparable ETASU that does not infringe? Put differently, how can a generic develop a comparable ETASU that meets the requirements for an ETASU set out in the FDAAA if it may not use the steps set out

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<sup>36</sup> 21 U.S.C. § 355-1(f)(3).

<sup>37</sup> U.S. Patent 8,112,290, *Methods for Delivering a Drug to a Hospital Patient for Short-Term Use While Minimizing Long-Term Use of the Drug* (Feb. 7, 2012).

in a brand company's patented ETASU, which was negotiated with the FDA in compliance with the requirements for ETASU under the FDAAA?

The problem with developing separate REMS with ETASU in such a case is that the generic cannot copy the patented system. Thus, the generic must develop a REMS with ETASU that omits at least one of the patented elements of the brand name drug maker's ETASU. This introduces two safety concerns. First, a single, shared system is likely to be less subject to confusion and error, as doctors and pharmacies will have only one program with which they have to work. Second, if the patented REMS with ETASU is the best and safest approach to distributing the drug, the generic will be prohibited from using the safest system.

Will brand manufacturers use their ETASU patents to keep generics off the market? Of course they will, and they already have. The incentive is too strong not to do so. Brand manufacturers have used their REMS with ETASU patents to hinder the generic manufacturer from moving forward with an ANDA.<sup>38</sup> Patent holders have refused to license their REMS systems, or have indefinitely stalled negotiations toward that end.<sup>39</sup>

By including REMS systems patents in the Orange Book, and by virtue of the steps required for a generic manufacturer to file its ANDA, the brand manufacturer compels the generic manufacturer to make a certification that the patent is invalid or will not be infringed by the marketing of the generic product (paragraph IV certification). This certification technically constitutes an infringement, giving the patent owner the right to file a patent infringement action, with an automatic stay that can potentially delay any generic launch for up to thirty months. There are questions as to whether Section 505's provision<sup>40</sup> for submitting patents claiming a method of using a drug for Orange Book listing applies to patents claiming an aspect of a REMS system.<sup>41</sup>

Brand companies have directly asserted their REMS with ETASU patents in infringement actions to keep generics off the market. In 2007, Celgene sued Barr Laboratories, which sought to make a generic version of Celgene's Thalomid.<sup>42</sup> Celgene alleged that approval of Barr's generic would infringe Celgene's REMS patents.<sup>43</sup> Celgene's complaint contains standard patent infringement language, for example: "Barr's submission of its ANDA . . . prior to the expiration of the '501 patent, constitutes infringement of one or more of the claims of that patent under 35 U.S.C. § 271(e)(2)(A)".<sup>44</sup>

Not only did Celgene seek to block Barr from using any REMS with ETASU system that would infringe Celgene's patented ETASU, Celgene also sought to block

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<sup>38</sup> For examples, see Adam C. Krol, Muna Abu-Shaar, *Safety, Innovation, or Access? REMS Creates Another Battlefield Between Branded and Generic Pharmaceuticals*, THE AIPLA ANTITRUST NEWS, at 5-14 (April 2015).

<sup>39</sup> *Id.*

<sup>40</sup> 21 CFR § 314.53(b)

<sup>41</sup> See Krol, et. al, *supra*, note 38, at 9.

<sup>42</sup> See Sarpatwari, et. al, *supra*, note 33.

<sup>43</sup> *Id.*

<sup>44</sup> CELGENE CORPORATION v. BARR LABORATORIES, INC. et al., Docket No. 2:07-cv-05485 (D.N.J. Nov 14, 2007), Court Docket.

FDA approval of any comparable ETASU. Celgene filed a citizen's petition demanding that the FDA refuse to approve any generic thalidomide because the use of any non-infringing REMS system would pose "unacceptable risks" by "compound[ing] the confusion and burdens associated with thalidomide risk management and mak[ing] it more likely that the system would be compromised."<sup>45</sup> In May 2010, Barr withdrew its application for generic thalidomide and Celgene subsequently dropped its suit, thus preventing a judicial decision on the merits of the patent infringement claim.<sup>46</sup>

Celgene is not alone in using patented REMS with ETASU to try to block generic entry to the market. In 2010, Jazz Pharmaceuticals filed suit against Roxane for infringement of its Orange Book-listed patents for Xyrem in response to Roxane's ANDA.<sup>47</sup> Roxane counterclaimed that Jazz's REMS patents were improperly listed in the Orange Book because they "all relate to a drug distributions system and method which utilized a central pharmacy and database to track all prescriptions for a sensitive drug and do not claim an approved method of using the drug."<sup>48</sup> This suit settled in April of 2017, again, before any judicial decision on the merits of the patent infringement or counterclaims.<sup>49</sup>

In 2013-15, Jazz separately sued Amneal Pharmaceuticals and Par Pharmaceuticals for infringement of its Orange Book-listed patents for Xyrem in response to their ANDAs.<sup>50</sup> Like Celgene's complaints, Jazz's complaints contained standard patent infringement language, for example: "Amneal's submission of its ANDA . . . , prior to the expiration of the '963 patent, constitutes infringement of one or more of the claims of that patent under 35 U.S.C. § 271(e)(2)(A)."<sup>51</sup> In 2014, Jazz sued Ranbaxy Laboratories and Watson Laboratories for infringement of Orange Book-listed patents for Xyrem in response to their ANDAs.

### **CREATES Act Is Narrowly Tailored Solution to Failure to Share ETASU**

The above shows that there is a persistent problem that has developed regarding misuse of ETASU patents to keep generics off the market. There is no solution to this problem under the status quo. Under the status quo, brand companies can use ETASU patents (however dubious their validity) in combination with citizen's petitions to both keep a generic from sharing a REMS with ETASU system, and to argue to the FDA that no generic can be sold without infringing the brand company's ETASU patent, which the brand company refuses to license.

Some may argue that the brand company has a right to exclude others from its patented ETASU, and that if that effectively extends a drug monopoly for many

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<sup>45</sup> Regulations.gov Celgene Corporation – citizen petition (September 20, 2007), available at (<https://www.regulations.gov/document?D=FDA-2007-P-0113-0002>).

<sup>46</sup> See Sarpatwari, et. al, *supra*, note 33, at 1477.

<sup>47</sup> See Krol, et. al, *supra*, note 38, at 11.

<sup>48</sup> Answer, Affirmative Defenses, and Counterclaims to Plaintiff's Complaint at 7, No. 2:10-cv-06108 (D. N.J. Dec. 29, 2010).

<sup>49</sup> Stipulation and Order of Dismissal No. 2:10-cv-06108 (D. N.J. April 11, 2017).

<sup>50</sup> See Krol, et. al, *supra*, note 38.

<sup>51</sup> JAZZ PHARMACEUTICALS, INC. et al v. AMNEAL PHARMACEUTICALS, LLC, No. 2:15-cv-01043 (D.N.J. Feb 06, 2015), Court Docket.

years, that is the tradeoff for the innovation in coming up with ETASU systems. This argument is not compelling, however. All of the REMS with ETASU patents that I have reviewed have tracked closely to the specific statutory requirements of the FDAAA. ETASU systems are not novel, innovative methods of protecting public safety. Rather, REMS with ETASU involve taking well-known and standard methods for ensuring the safe distribution of dangerous drugs, and applying them to the specific risks and populations at issue for a specific drug. Given that, the REMS with ETASU patents all seem likely to be vulnerable to obviousness attacks.

But even if some REMS with ETASU are innovative, they are different than, say, a patent on a new electrical engineering standard. REMS programs are protocols to ensure safe distribution of drugs. The incentive for creating the program is to be allowed to sell the drug, not to be able to sell the REMS program itself. Thus, creators of REMS programs already have adequate incentive to invent these programs without any patent grant. I've argued in earlier work that in such cases, we should be skeptical about allowing patents at all.<sup>52</sup> Accordingly, it would be reasonable for Congress to disallow patents for REMS. Rather than taking this approach, however, the CREATES Act effectively requires a brand company to either license a generic to participate in its patented REMS with ETASU under fair and reasonable terms, or to not object to the use of a comparable system.

The CREATES Act requires that the brand company agree to a single, shared REMS with ETASU within 120 days of a request by a generic. The Act provides for civil liability if the brand company fails to agree by this time. Some may argue that 120 days is not enough time, but given that the FDAAA gives a brand company 120 days to design an ETASU in the first place, 120 days should be more than adequate merely to agree how to share an ETASU that has already been designed and approved.

If the brand company does not reach agreement by the deadline, it is liable for: (a) an injunction requiring it to share its ETASU system, (b) attorneys' fees, and (c) money damages sufficient to deter the refusal to share, not to exceed the revenue for the drug during the period of refusal. The Act does not require the brand company to share if the Secretary has granted a waiver from the single, shared REMS with ETASU requirement. Thus, the Act will stop the abuse of REMS with ETASU patents to keep generics off the market. Unless the Secretary grants a waiver, the brand company will have to share its ETASU (on commercially reasonable terms that require sharing the cost of the system, and may include a premium for the patent license). If the brand company does not want to share, then it cannot argue that the generic should not receive a waiver, because any non-patented ETASU would be unsafe. If the brand company makes this argument, it will effectively be saying that only its patented ETASU is appropriate, and thus, under the Act, it will be forced to share the patented ETASU.

This forced sharing of an ETASU when no other alternative is as safe is a very good thing. The entire point of the FDAAA's REMS with ETASU requirements is to ensure that dangerous drugs that can have substantial benefit when used correctly

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<sup>52</sup> David S. Olson, *Taking the Utilitarian Basis of Patent Law Seriously: The Case for Restricting Patentable Subject Matter*, 82 Temp. L. Rev. 181 (2009).

are distributed to the public as safely as possible. It would be poor public policy to allow a brand company to monopolize safety and thus either endanger the public or prevent the launch of generics after a patent has expired.

#### IV. Consideration of Critiques of the CREATES Act

A number of criticism have been leveled at the CREATES Act. I have looked for any criticisms I could find, and I will now address the most pertinent critiques.

A. *Brand companies should be able to refuse to sell to generics because the brand company could be liable for any misuse of the drug or failure to comply with REMS on the part of the generic.*

Some have argued that brand companies should be able to refuse to sell to generics because, even under the CREATES Act, the brand companies could face liability for misuse of the drug by generics.<sup>53</sup> This argument has very little merit. First, the CREATES Act specifically exempts a brand company from liability for sharing with a generic when there is no REMS program, or once the Secretary has approved the protocols of the generic in the case of drugs covered by REMS. Second, products liability claims arising from misuse or negligence on the part of the generic will lie against the generic, not against the brand. Only if the brand learns of safety information that it withholds from the market, or itself misuses the drug will the brand be liable. Third, some have argued that brand companies could have their reputations sullied if generics sell unsafe drugs or do not follow safety protocols. But there is no evidence that the public cannot distinguish between brand and generic drugs. Moreover, brand companies could use any safety lapse on the part of generics to encourage doctors to prescribe the branded version of the drug.

B. *Thirty days is too short a time to negotiate the sale of samples.*

Some have argued that thirty days is too short a period to negotiate the sale of samples.<sup>54</sup> For small molecule drugs, this is without merit. The statute already exempts the requirement that a brand company directly supply the listed drug if the drug is available through an unrestricted wholesaler, or in cases of short-term shortages. Otherwise, providing the number of samples required for small molecule testing may not be much different than providing the needs of a single drugstore outlet on a single day. There is no more to be done than to agree upon a price and to ship the drugs. Because the drugs are already being sold, market prices are readily available. Nor is a generic likely to quibble much if it is charged on the upper end of the market, given that the cost of samples is generally a small part of an ANDA application.

When it comes to large molecule biosimilars, the fact that a much larger quantity of samples is needed, over a longer period of time, may mean that the negotiations are a bit more complicated. For biosimilars, the parties must agree on the quantity of samples, and on the schedule upon which they are to be delivered.

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<sup>53</sup> See, e.g., Testimony of Peter Safir, *supra*, note 24.

<sup>54</sup> See, e.g., Lietzan, *supra*, note 25.

This is still a relatively simple agreement, but it is a bit more complicated than an agreement for small molecule drugs. From my research, 30 days seems to be sufficient, but if the period is extended to, say, 45 days, I see no reason why that would cause significant harm to generics seeking samples.

One should note that the CREATES Act does away with any arguments that the brand company must engage in negotiations to ensure the safe use of its drugs. Because the Act exempts the brand company from liability for selling samples to approved generics, the brand company need not include any provisions on use of the drug in its sales contracts.

*C. 120 days is too short a time to agree to a single, shared REMS with ETASU*

Some have argued that 120 days is too short a time to agree on a single, shared REMS with ETASU system.<sup>55</sup> This ignores the fact that the FDAAA gives a drug company only 120 days to come up with the entire ETASU system in the first place. If this is long enough to design the system, there is no reason that this should not be long enough to negotiate how to add generics to the system, and how to allocate the costs of the system.

*D. Generics will game the system to receive windfall damages awards from brand companies*

Some have argued that generics will game the system set up by the CREATES Act to extract large money damages from brand companies.<sup>56</sup> The argument is that generics will request samples, or request access to a REMS with ETASU, and then fail to negotiate in good faith. Instead, the generic will wait for the 30 or 120 days, respectively, to expire, and continue to not reach an agreement, until a substantial amount of time has passed. The generic will then sue for money damages for the brand company's refusal to share. Because damages can be up to the revenue for the drug, the generics can then collect millions or hundreds of millions of dollars from the brand company for doing nothing.

This parade of horrors is highly unlikely to occur. First, the CREATES Act only provides monetary liability if a brand company's refusal to share was "without a legitimate business justification." Any situation in which a brand company negotiates in good faith and a generic refuses to accept any reasonable offer will be enough to avoid monetary liability for the brand company. In addition, the damages award is within the discretion of the court to deter bad behavior on the part of the brand company. There is no requirement that the court award anywhere near the maximum award of all revenues during the period of refusal if the drug is a high-revenue drug. Nor would a court have a justification to do so if the generic were gaming the system.

It is true that the possibility of monetary damages gives the generic some additional power in negotiating. This may result in the generic getting favorable prices for samples, or not shouldering as much of the cost of the REMS with ETASU

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<sup>55</sup> *Id.*

<sup>56</sup> *Id.*

(such as auditing costs, etc.). Given, however, that the samples must be sold at market-based prices, and that it would be legitimate for a brand company not to agree to share a REMS if it bears all of the costs, this additional bargaining power given to generics by the Act seems modest and unlikely to have significant effect on the market for developing and distributing drugs.

*E. Generics can get samples from outside the U.S.*

Some have argued that the CREATES Act is unnecessary because generics can get samples from outside the United States.<sup>57</sup> Brand drugs are not always available outside of the U.S., however. Moreover, formulations in other countries are not always the same as in the U.S. Most importantly, however, the FDA has said that such samples will not suffice.<sup>58</sup> Thus, this argument against the CREATES Act is without merit.

*F. Forcing a brand company to sell samples is against patent or antitrust policy.*

Finally, some have argued that forcing a brand company to sell samples violates patent law policy or antitrust policy, which supposedly gives a patent owner a sacrosanct right not to sell its patented product to certain customers.<sup>59</sup> This is incorrect. While it is true that generally a patent owner has no obligation to practice its patent, just as a business generally has no duty to deal with rivals, nothing in patent law overrules antitrust law on duties to deal. In fact, the Supreme Court has not hesitated to require a patent owner to sell its patented goods without discrimination, including to competitors, when competition required it. In *Eastman Kodak Co. v. Image Technical Servs., Inc.*, 504 U.S. 451 (1992), the Court forced Kodak to sell its patented copy machine parts to competing repair service providers to avoid an anticompetitive result. This is in accord with longstanding Supreme Court precedent that there is no general right to refuse to deal.<sup>60</sup> In the case of brand companies being forced to share samples, they are not being forced to dust off and practice an unused patent. Instead, what they are being asked to do is to not discriminate in anticompetitive ways regarding to whom they sell their products. This is well within accepted antitrust and patent law principles.

I agree with other commentators that the CREATES Act is an elegant, narrowly tailored fix to the problem of anticompetitive abuse of FDA regulations

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<sup>57</sup> *Id.*

<sup>58</sup> Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 Guidance for Industry, *available at* <https://www.fda.gov/downloads/drugs/guidances/ucm444661.pdf> (“At this time, as a scientific matter, it is unlikely that clinical comparisons with a non-U.S.-licensed product would be an adequate basis to support the additional criteria required for a determination of interchangeability with the U.S.-licensed reference product.”).

<sup>59</sup> *Id.*

<sup>60</sup> See, e.g., *United States v. Colgate & Co.*, 250 U.S. 300, 307 (1919) (A business may freely choose with whom to deal except where its motivation is to obtain or maintain a monopoly.); *Aspen Skiing Co. v. Aspen Highlands Skiing Corp.*, 472 U.S. 585, 601 (1985) (“The high value ... placed on the right to refuse to deal with other firms does not mean the right is unqualified”).

that is superior to relying on antitrust law.<sup>61</sup> But if the CREATES Act, or something like it, is not passed, the only tool available to generics and the FTC will be antitrust law. Antitrust law may well apply to refusals to share, because unlike in *Verizon v. Trinko*, 540 U.S. 398 (2004), the statutory scheme present in the FDAAA does not specifically deal with the anticompetitive conduct of refusing to deal. Thus, the correct analogy is not *Trinko*, but *Otter Tail Power Co. v. United States*, 410 U.S. 366 (1973), in which the Court allowed antitrust law to supplement a statutory scheme to prevent anticompetitive conduct. Thus, if the CREATES Act or something like it is not passed, antitrust suits might be brought to force sharing, and this will be an inferior solution due to the lengthy nature of such suits and the complex issues presented.<sup>62</sup> A narrow statutory solution is much superior to leaving this to the vagaries, uncertainties, and expense of antitrust suits.

Thank you for inviting me to testify on these important matters. I am happy to answer any questions the subcommittee might have.

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<sup>61</sup> See Written Testimony of Alden F. Abbott before the U.S. Senate Judiciary Committee Subcommittee on Antitrust, Competition Policy, and Consumer Rights, at 4-5 (June 21, 2016), available at <https://www.judiciary.senate.gov/imo/media/doc/06-21-16%20Abbott%20Testimony.pdf>

<sup>62</sup> *Id.*