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Higher Drug Prices from Anticompetitive Conduct: Three Case Studies

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Abstract. U.S. consumers pay high drug prices. Brand-name drug companies claim that these prices are justified by pathbreaking research and development. But, sometimes the prices result from anticompetitive conduct. This article offers three case studies of how such behavior can increase price based on wakefulness drug Provigil, the allergic-reaction-treating EpiPen, and infection-treating Daraprim. The article contends that behavior that makes no sense other than by harming a competitor, that undercuts a regulatory regime, or that involves collusive conduct should not be protected. In targeting this behavior, antitrust scrutiny promises to lower drug prices.

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U.S. consumers pay high drug prices. Brand-name drug companies claim that these prices are justified by pathbreaking research and development. But sometimes the prices result from anticompetitive conduct. This article offers three case studies of how such behavior can increase price.

The article first introduces wakefulness drug Provigil, for which Cephalon paid $300 million to generics to delay entering the market while it introduced nearly-identical successor Nuvigil. It then discusses the epinephrine-injecting EpiPen, for which Mylan engineered sustained price increases at the same time it engaged in a patent settlement, filed a "citizen petition," and entered into exclusive contracts with schools. Finally, it discusses infection-treating Daraprim, for which the price rose 5000% after the company significantly restricted its distribution system and denied samples needed to enter the market.

I. CASE STUDY 1: PROVIGIL

A. Facts

Provigil demonstrates how brand firms can combine multiple forms of anticompetitive conduct. Provigil is a sleep-disorder medication marketed by Cephalon. It was initially approved for excessive daytime sleepiness associated with narcolepsy and was subsequently used to treat obstructive sleep apnea and shift work sleep disorder.[1] U.S. soldiers, particularly those fighting in the Iraq War, have used it to stay awake for as long as 40 hours at a time.[2] The drug is considered the "gold standard" for the treatment of the excessive sleepiness accompanying sleep disorders.[3] U.S. sales of Provigil increased from $25 million in 1999 to $475 million in 2005 to $800 million in 2008.[4]

The active ingredient in Provigil is a chemical compound called modafinil.[5] Cephalon filed a New Drug Application for Provigil in 1996, which the FDA approved in 1998.[6] The U.S. patent covering modafinil was issued in 1979 and expired in 2001.[7] Cephalon obtained a second patent in 1997. This patent covered a formulation of modafinil that

[1] Complaint for Injunctive Relief at 7, Federal Trade Commission v. Cephalon, Inc., No. 08-cv-00244 (JDB), (D.D.C. Feb. 14, 2008), ECF No. 1. [hereinafter Cephalon Compl.].
[2] *Id.*
[3] Tom Spears, *New Drug May Help Soldiers Stay Awake*, OTTAWA CITIZEN, Oct. 11, 2003, http://www.modafinil.com/article/soldiers.html; Cephalon Compl., *supra* note 1, at 7.
[4] Cephalon Compl., *supra* note 1, at 8.
[5] *Id.* at 7.
[6] *Id.*
[7] *Id.* at 8.

consisted of a specified distribution of small particles.[8] This narrower patent lasted until October 2014, with Cephalon receiving an additional six months of pediatric exclusivity extending protection to April 2015.[9]

Unlike the patent on the compound itself, generic firms could, without difficulty, avoid this narrow formulation patent. As a consultant advised Cephalon in 2002: "[A]ll generic companies know" that the patent "may be easily circumvented" by manufacturing products to contain a different distribution of modafinil particle sizes.[10] Given the ease with which generic firms could circumvent the particle-size patent, it is no surprise they were eager to do so. On the first day that the FDA could accept a generic application for Provigil, four companies—Teva, Ranbaxy, Mylan, and Barr—did so.[11]

Cephalon sought to maintain its market share by introducing a successor product, Nuvigil, in 2006.[12] The longer-lasting Nuvigil was similar to Provigil in many ways, including chemical composition.[13] It offered modest improvements by allowing patients to take a pill once (instead of twice) a day.[14] The FDA, however, had not approved Nuvigil by late 2005. And "there was considerable uncertainty as to whether the FDA would approve Nuvigil early enough in 2006 to enable Cephalon to successfully migrate customers from Provigil to Nuvigil before the entry of a generic version of Provigil."[15] Given this uncertainty, Cephalon decided to settle patent litigation with the four first-filing generics.[16] Cephalon paid more than $300 million to the four generics to agree to forgo entry until April 2012.[17]

B. Interplay: The Big Picture

The primary agency charged with enforcing the antitrust laws in the pharmaceutical industry, the Federal Trade Commission (FTC), brought an antitrust case against Cephalon, alleging that the company "knew that generic Provigil entry would lead to substantial declines in the

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[8] *Id.*

[9] Cephalon, *Cephalon Granted Six Months of Pediatric Exclusivity for Provigil*, Mar. 28, 2006, http://www.cephalon.com/media/news-releases/product/provigil/article/cephalon-granted-six-months-of-pediatric-exclusivity-for-provigilr/.

[10] Cephalon Compl., *supra* note 1, at 9.

[11] *Id.*

[12] *Id.* at 13.

[13] Cephalon, *Cephalon Receives FDA Approval of Nuvigil for the Treatment of Excessive Sleepiness Associated with Three Disorders*, June 18, 2007, http://www.cephalon.com/media/news-releases/by-product/product/nuvigil/article/cephalon-receives-fda-approval-of-nuvigiltm-for-the-treatment-of-excessive-sleepiness-associated-w/.

[14] David Phillips, *The 10Q Detective: Losing Sleep over Cephalon*, BLOOMBERG, Sept. 28, 2009, https://www.bloomberg.com/news/articles/2009-09-28/the-10q-detective-losing-sleep-over-cephalon.

[15] Cephalon Compl., *supra* note 1, at 13-14.

[16] *Id.* at 14.

[17] *Id.* at 2.

company's revenues."[18] A Cephalon vice president, for example, projected a 75-90% price reduction that would lower revenues by more than $400 million (nearly 75% of the drug's annual sales) within one year.[19] The generic firms estimated a similar impact, with Teva, for example, projecting that generic versions "would garner 90% of all modafinil prescriptions within a month."[20] In fact, the Cephalon CEO himself conceded that the settlements provided "six more years of patent protection," that resulted in "$4 billion in sales that no one expected."[21] *Interplay: The Big Picture*.

In its motion to dismiss the complaint, the defendant noted that the settlement, which allowed entry in 2012, "resulted in generic entry *years earlier* than patent expiration" in 2015.[22] A bird's-eye view of the activity, however, shows how the various forms of anticompetitive behavior fit together. Cephalon had no intention of competing in a robust market with generics in 2012. The generics themselves, in obtaining more than $300 million from Cephalon, did not expect vibrant competition in 2012.

Rather, by delaying the potential onset of generic competition until 2012, for six years after settlement, Cephalon bought itself a period in which it was *guaranteed* that its weak Provigil patent would not be challenged. With that certainty in hand, Cephalon could enjoy the luxury of an extended period in which it could switch the market to its new sleepiness drug, Nuvigil. Nuvigil, which the FDA approved in 2007, enjoys patent protection until 2023.[23]

A Cephalon spokesman conceded that, after settlement, "[t]he pressure is not what it was" and that the company was not required "to make a quick transition from Provigil to Nuvigil."[24] And an industry analyst agreed that the delay would "allow Cepahlon to seek to expand its wakefulness franchise" rather than treating Nuvigil "merely as a conversion opportunity … that would be under pressure to establish itself early."[25]

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[18] *Id.* at 10.
[19] *Id.*
[20] *Id.*
[21] *Id.* at 2.
[22] Defendant Cephalon, Inc.'s Memorandum of Points and Authorities in Support of its Motion to Dismiss at 26, Federal Trade Commission v. Cephalon, Inc., No. 08-cv-00244 (JDB) (D.D.C. May 2, 2008), ECF No. 17.
[23] *Cephalon Receives FDA Approval Of Nuvigil(TM) for the Treatment of Excessive Sleepiness Associated with Three Disorders*, MEDICAL NEWS TODAY, June 19, 2007, http://www.medicalnewstoday.com/articles/74585.php.
[24] Robert Steyer, *Cephalon Puts Worries to Rest*, THESTREET.COM, July 14, 2006, http://www.thestreet.com/print/story/10268224.html.
[25] Cephalon, Inc., Q1 2009 Earnings Call Transcript, SEEKING ALPHA, May 5, 2009, http://seekingalpha.com/article/135541-cephalon-inc-q1-2009-earnings-call-transcript?page=-1.

C. Specific Strategy

Cepahlon's switching strategy had two simple components: making Provigil less desirable and making Nuvigil more desirable. The easiest way to make Provigil less desirable was to increase its price. And that is what it did, leaving nothing to chance. Between 2004 and 2008, Cephalon increased the price of Provigil by 74%.[26] As a Cephalon vice president conceded: "[W]e will likely raise Provigil prices to try to create an incentive for the reimbursers to preferentially move to Nuvigil."[27]

Another means to reduce Provigil's attractiveness was to stop promoting it. And that is what it did. Cephalon officials explained that they "actually pulled all promotion from Provigil" after the first quarter of 2009 "in anticipation of the [Nuvigil] launch," which occurred in June.[28] Specifically, Cephalon pulled all samples, promotional materials and messaging on Provigil in order to replace them with new materials and samples on Nuvigil.[29]

Having weakened the competitive position of Provigil, Cephalon set off on its second task: promoting Nuvigil. Here too it left no stone unturned. The CEO sang Nuvigil's praises: "With an extensive clinical program supporting Nuvigil, and a patent that extends to 2023, we believe that Nuvigil will be a very successful product that will ultimately benefit more patients than Provigil."[30] The company brought out the heavy promotion artillery: "Our sales force is trained and performing all the necessary pre-launch activities to ensure a successful launch."[31] Bringing it all together was the "excitement" in the marketplace from the cheaper, "more effective" Nuvigil. Revealing all too little of its role in increasing Provigil's price, Cephalon played coy in being "particularly pleased to offer Nuvigil at a discount to Provigil."[32]

By switching the market from a drug about to confront generic entry to a new patent offering nearly 20 additional years of protection, Cephalon kept prices much higher than they otherwise would have been. Prices typically fall dramatically when generics enter. Markets

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[26] Jonathan D. Rockoff, *How a Drug Maker Tries to Outwit Generics*, WALL ST. J., Nov. 17, 2008, http://rianjs.net/media/2008/How%20a%20Drug%20Maker%20Tries%20to%20Outwit%20Generics.pdf.

[27] *Id.*

[28] Cepahlon Q1 2009 transcript, *supra* note 25.

[29] Cephalon, Inc., Q2 2009 Earnings Call Transcript, SEEKING ALPHA, Aug. 4, 2009, http://seekingalpha.com/article/153789-cephalon-inc-q2-2009-earnings-call-transcript?page=-1.

[30] Cephalon, Inc., Q4 2008 Earnings Call Transcript, SEEKING ALPHA, Feb. 13, 2009, http://seekingalpha.com/article/120423-cephalon-inc-q4-2008-earnings-call-transcript?page=-1.

[31] Cepahlon Q1 2009 transcript, *supra* note 25.

[32] *Id.*

with two generics witness prices roughly half the brand price, and those in which six or more generics enter see the price fall to a quarter of the brand price.[33] Cephalon's CEO conceded that settlements that delayed generic versions of Provigil between 2006 and 2012 cost consumers $4 billion, with this figure not even including the costs suffered by patients who switched to patent-protected Nuvigil after 2012. Cephalon's switch from Provigil to Nuvigil, undertaken in the context of its settlement with four generic firms that were no longer able to challenge its patent, reveals how a manufacturer can increase price through the combination of settlements and product hopping.

II. EPIPEN: SETTLEMENT, PETITION, EXCLUSIVE CONTRACTS

Conduct related to Mylan's EpiPen also threatens anticompetitive behavior, albeit through a different combination of activity: settlements, citizen petitions, and exclusive contracts.

A. Background

In the summer of 2016, Mylan found itself under fire for high EpiPen prices. Between 2009 and 2016, Mylan had raised the price of this life-saving device, which delivers epinephrine to treat anaphylaxis shock, 15 times, resulting in an increase of more than 400%.[34] The medicine in an EpiPen costs only pennies per dose.[35] But a pack of two, which needs to be replaced each year, and which families buy in multiple quantities for various locations, costs more than $600.[36] The consequences of these prices are felt in all corners, as life-threatening allergies from peanuts, shellfish, and other substances affect fifteen million Americans and 1 in 13 children.[37]

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[33] FDA, Generic Competition and Drug Prices, Nov. 28, 2017, https://www.fda.gov/Aboutfda/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm.

[34] Sy Mukherjee, *How Mylan Got Away With Its Enormous Price Hike for the EpiPen*, FORTUNE, Aug. 22, 2016, http://fortune.com/2016/08/22/mylan-epipen-price-hike-monopoly/; Matt Egan, *How EpiPen Came to Symbolize Corporate Greed*, CNN MONEY, Aug. 29, 2016, http://money.cnn.com/2016/08/29/investing/epipen-price-rise-history/.

[35] Letter from Jason Chaffetz (R-UT) & Elijah E. Cummings (D-MD) to Heather Bresch, Aug. 29, 2016, http://democrats.oversight.house.gov/sites/democrats.oversight.house.gov/files/documents/2016-08-29%20JC%20and%20EEC%20%20to%20Bresch-Mylan%20EpiPen%20Pricing.pdf (questioning price increase and commencing congressional investigation).

[36] *Id.*

[37] Mukherjee, *supra* note 34, at 1.

Although many reasons were offered for the price hike (such as a slow-moving FDA approval process[38] and convoluted distribution chain[39]), Mylan cleared the field of competitors through at least three potentially anticompetitive actions that exploited (1) the litigation process through settlement, (2) the administrative process through citizen petitions, and (3) the laws requiring auto-injectors in schools through exclusive contracts.

B. Settlement

The first activity involved settlement. In August 2009, Meridian Medical Technologies (a Pfizer subsidiary that manufactures the EpiPen) and King Pharmaceuticals (which acquired Meridian) sued Teva for patent infringement.[40] After a four-day bench trial in early 2012,[41] the parties settled in April 2012,[42] only weeks before post-trial briefings were due in late May 2012.[43] While the terms of the settlement are confidential, a Mylan press release confirms that Teva agreed to delay entering the market for more than three years, until June 2015.[44] During the period in which Teva could not enter the market, EpiPen prices more than doubled, from (roughly) $220 to $460.[45]

One cannot know with certainty how the court would have decided the patent litigation. But ominous tea leaves on the patents' validity are revealed by the court's *Markman*[46] claim construction hearing, which signaled greater success for Teva than for the patent owners.[47] The settlement also was concerning, not just because it delayed a successful

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[38] *See, e.g.*, Rand Paul, *Sen. Rand Paul: EpiPen Scandal Is a Perfect Example of Crony Capitalism*, TIME (Sept. 7, 2016), http://time.com/4482179/sen-rand-paul-epipen-scandal/.

[39] Dan Mangan & Anita Balakrishnan, *Mylan CEO Bresch: 'No One's More Frustrated Than Me' About EpiPen Price Furor*, CNBC, Aug. 25, 2016, http://www.cnbc.com/2016/08/25/mylan-expands-epipen-cost-cutting-programs-after-charges-of-price-gouging.html.

[40] Complaint, King Pharm., Inc. et al v. Teva Parenteral Med. Inc. et al, No. 09-652-GMS (D. Del. Aug. 28, 2009), ECF No. 1.

[41] Official Transcript of Trial, King Pharm., Inc. et al v. Teva Parenteral Med. Inc. et al, No. 09-652-GMS, (D. Del. July 25, 2012), ECF 150-54.

[42] *See Mylan and Pfizer Announce Epinephrine Auto-injector Settlement Agreement with Teva*, (Apr. 26, 2012), http://newsroom.mylan.com/pressreleases?item=123144.

[43] Proposed Order Regarding Post-Trial Submissions, King Pharm., Inc. et al v. Teva Parenteral Med. Inc. et al, No. 09-652-GMS (D. Del. Apr. 12, 2012), ECF No. 146.

[44] *Id.*

[45] *See* Dan Mangan, *This Chart Shows Why Everyone's Angry About Soaring Price of Lifesaving EpiPen*, CNBC, Aug. 23, 2016, http://www.cnbc.com/2016/08/23/this-chart-shows-you-why-a-lot-of-people-are-angry-about-the-price-of-epipen.html (providing figures from July 2012 and May 2015).

[46] *See generally* Markman v. Westview Instruments, Inc., 517 U.S. 370 (1996) (holding that claim construction is a matter of law and that judges are to construe the meaning of patent claims).

[47] *See* Michael A. Carrier & Carl. J. Minniti III, *The Untold EpiPen Story: How Mylan Hiked Prices by Blocking Rivals*, 102 CORNELL L. REV. ONLINE 53, 61-62 (2017).

generic from the market, but also because of its effects on other, later-filing generics. The Hatch-Waxman Act awards 180 days of exclusivity to the first generic to challenge a brand firm's patent claiming that it is invalid or not infringed.[48] This period does not begin until the first-filing generic enters the market, in this case three years in the future. Because Teva was the first filer,[49] as a result of delaying Teva's entry into the market, Mylan and its partners delayed *all generics* that sought to file applications based on the EpiPen.[50]

Settlements of patent litigation threaten potential landmines of anti-competitive effects. The Supreme Court made clear in *FTC v. Actavis*[51] that a settlement by which a brand pays a generic to delay entering the market could have "significant adverse effects on competition" and violate the antitrust laws.[52] Although the *Actavis* decision post-dated the settlement, the parties likely were aware at the time they settled in April 2012 that potentially rigorous scrutiny was on the horizon.[53]

Because the terms of the settlement are confidential, it is not possible to know whether there was a transfer of consideration to Teva. But the generic-friendly claim construction bolstering Teva's leverage, together with the vast scale of the market, increased the likelihood that Meridian delayed Teva's entry through payment.

C. Citizen Petition

In addition to delayed-entry settlements, Mylan sought to forestall Teva's entry by employing a "citizen petition," which is meant to raise safety concerns with the FDA but which has been used by brand firms to delay generic entry. As I have shown, "citizen" petitions are filed mostly by brand firms, and are almost always (92%) denied.[54]

Mylan filed its citizen petition against Teva's Abbreviated New Drug Application (ANDA or generic application) in January 2015.[55] A

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[48] 21 U.S.C. §355(j)(5)(B)(iv) (2012).

[49] *Update: Teva and Antares's Generic Challenge to Epi-Pen*, SEEKING ALPHA, Feb. 23, 2012, http://seekingalpha.com/article/388681-update-teva-and-antaress-generic-challenge-to-epipen.

[50] *See* Michael A. Carrier, *Payment After Actavis*, 100 IOWA L. REV. 7, 15 (2014).

[51] 570 U.S. 136 (2013).

[52] *Id.* at 148.

[53] Oral Argument, *In re* K-Dur Antitrust, et al, Nos. 10-2077, 10-2078, 10-2079, & 10-4571, at 25, 36, 37 (3d Cir. Dec. 12, 2011). *See* Carrier & Minniti, *supra* note 47, at 62 (describing how appeal would be heard by Third Circuit and how settlement was signed shortly after that court's December 2011 oral argument in *In re K-Dur Antitrust Litigation*, in which judges expressed skepticism about arguments for minimal antitrust scrutiny).

[54] Michael A. Carrier & Carl Minniti, *Citizen Petitions: Long, Late-Filed and At-Last Denied*, 66 AM. U. L. REV 305, 333 (2016) (examining all 505(q) petitions (which ask the FDA to take action against a pending generic application) filed between 2011 and 2015).

[55] Citizen Petition from Mylan Specialty, L.P., Docket No. FDA-2015-P-0181-0001 at *1 (posted on Jan. 16, 2015).

response from the FDA was anticipated no later than June 2015[56]—only weeks before Teva was permitted to enter the market pursuant to its settlement. As my study revealed, Mylan's petition appears to have been filed as a delay tactic to avoid generic approval and the loss of its overwhelming share of the market.[57]

Just as concerning, in May 2015, four months after filing the petition, Mylan filed a supplemental study asserting that patients would not be able to operate Teva's proposed device without retraining.[58] Experts explained, however, that Mylan's supplemental study "had a lot of problems" as it "lacked a control group; did not study the actual generic but a prototype instead; used a small number of participants; failed to provide them with proper instructions for use; and told participants to watch a video rather than actually use the Teva device."[59]

Shedding even more light on the questionable petition and supplemental study is the timing. In a development of which the industry would be keenly aware, Teva filed its ANDA against the Epi-Pen in 2008.[60] And court documents show that Teva produced its ANDA filing in the course of litigation in September 2010.[61] This material included "detailed product descriptions, drawings, and instructions for use" for Teva's proposed generic.[62]

At the time (and to this day), Mylan was working hand-in-hand with Meridian/King, with the former taking over Orange Book sponsorship of the drug application and the latter targeting rivals in litigation. It thus seems exceedingly likely that Mylan would have been aware of Teva's ANDA in 2008 and aware of documents explaining Teva's product in 2010. In fact, it was *Mylan* that announced the settlement of the litigation, confirming its close connection to the case. This connection raises significant concerns that Mylan waited more than four years to file its citizen petition in 2015.

It is reasonable to conclude that Mylan's (1) filing of a petition years after invariably knowing about Teva's generic, (2) filing of a

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[56] *See* 21 U.S.C. § 355(q)(1)(F) (2012) ("The Secretary shall take final agency action on a petition not later than 150 days after the date on which the petition is submitted.").

[57] *See* Carrier & Minniti, *supra* note 54, at 350-51.

[58] Supplement from Mylan Specialty, L.P., Docket No. FDA-2015-P-0181-0007 at *10 (posted on May 5, 2015).

[59] Ed Silverman, *How Mylan Tried to Keep Teva from Selling a Generic EpiPen*, STAT, Aug. 31, 2016, https://www.statnews.com/pharmalot/2016/08/31/mylan-teva-generic-epipen/.

[60] Larry Smith, *The Promise of the Antares Pipeline is the Basis of My Buy Recommendation*, SMITH ON STOCKS, Jan. 25, 2012, https://smithonstocks.com/the-promise-of-the-antares-pipeline-is-the-basis-of-my-buy-recommendation-ais-2-40/.

[61] Defendants' Brief in Support of their Motion to Dismiss, King Pharm., Inc. v. Teva Parenteral Med. Inc., Case No. 09-652-GMS at 6 (D. Del., filed Dec. 13, 2010).

[62] *Id.*

petition calculated to delay entry after settlement, and (3) late-filing of a supplemental study comprised a strategy to delay Teva's ANDA approval *beyond* the already-*delayed* agreed entry date of June 2015. Although the FDA is required to respond to petitions within 150 days, on numerous occasions the agency offers only an interim response explaining that it requires more time due to "complex issues raised" in the petition.[63] As a result, a strategy similar to the one Mylan used easily could have pushed a petition's disposition (and thus generic approval) past 150 days. For a billion-dollar drug product like the EpiPen, each day of delay meant an extra $3 million.

Parties filing petitions with government agencies often can rely on the immunity from the antitrust laws provided by the *Noerr-Pennington* doctrine, as "[t]hose who petition [the] government for redress are generally immune from antitrust liability."[64] But this defense is not absolute. In particular, there is a well-established "sham" exception, which could be satisfied in this case by Mylan's likely longstanding knowledge of Teva's generic, the timing of the petition in relation to the settlement, and the questionable nature of the supplemental study.[65] On a broader level, the petition could be viewed as an integral part of an overall scheme of monopolization, together with settlement and (as discussed immediately below) exclusive dealing.[66]

D. Exclusive Dealing

In addition to delaying *future* generic entry from Teva (and others waiting in line behind it) through settlement and petition, Mylan blocked *present* competitors through its program for distributing the EpiPen to schools.[67]

In November 2013, in response to a seven-year-old girl at a Virginia school dying from an allergic reaction to peanuts,[68] Congress

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[63] *E.g.*, Interim Response Letter from FDA CDER to Cubist Pharm., Inc., Docket No. FDA-2015-P-1595-0004 (posted on Oct. 26, 2015).

[64] Prof'l Real Estate Investors, Inc. v. Columbia Pictures Indus., 508 U.S. 49, 56 (1993).

[65] *E.g.*, Tyco Healthcare Group v. Mutual Pharm., 762 F.3d 1338, 1348 (Fed. Cir. 2014); *In re* DDAVP Direct Purchaser Antitrust Litig., 585 F.3d 677, 694 (2d Cir. 2009); *In re* Flonase Antitrust Litig., 795 F. Supp. 2d 300, 317 (E.D. Pa. 2011); *In re* Prograf Antitrust Litig., 2012 WL 293850, at *5 (D. Mass. Feb. 1, 2012).

[66] *See, e.g.*, *In re* Neurontin Antitrust Litig., 2009 WL 2751029, at *15 (D.N.J. Aug. 28, 2009).

[67] The New York Attorney General launched an antitrust investigation of this conduct. Press Release, *N.Y. Attorney General, A.G. Schneiderman Launches Antitrust Investigation into Mylan Pharmaceuticals Inc., Maker of EpiPen*, Sept. 6, 2016, http://www.ag.ny.gov/press-release/ag-schneiderman-launches-antitrust-investigation-mylan-pharmaceuticals-inc-maker.

[68] Cynthia Koons & Robert Langreth, *How Marketing Turned the EpiPen into a Billion-Dollar Business*, BLOOMBERG BUSINESSWEEK, Sept. 23, 2015, https://www.bloomberg.com/news/articles/2015-09-23/how-marketing-turned-the-epipen-into-a-billion-dollar-business.

passed the School Access to Emergency Epinephrine Act.[69] Under this law, the Secretary of the Department of Health and Human Services is authorized to give preferential funding to states with schools that maintain an emergency supply of epinephrine for students.[70] The law has had a significant effect: 11 states require[71] and 38 encourage[72] schools to stock epinephrine.[73] This federal legislation has been supplemented by state laws that mandate that public schools obtain autoinjectors.[74]

On one hand, such an arrangement could increase access to a life-saving device. But on the other, it could exclude competitors. As a condition of receiving discounted EpiPens,[75] schools were required to agree that they would "not in the next twelve (12) months purchase any products that are competitive to EpiPen® Auto-Injectors."[76] The language appeared in order forms in August 2014, June 2015, and April 2016,[77] and Mylan has admitted such a practice.[78]

In antitrust terms, this conduct offers a discount price based on exclusivity. As the leading treatise explains, such an arrangement "should generally be treated as no different from an orthodox exclusive-dealing arrangement."[79] Exclusive dealing case law stems from Section 3 of the Clayton Act, which prohibits a "discount … or rebate … on the condition, agreement, or understanding that the … purchaser … shall not use or deal in the goods … of

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[69] Pub. L. No. 113-48, 127 Stat. 575 (2013) (codified at 42 U.S.C. § 280g(d)(1)(F)–(G)).

[70] *Id.*

[71] *School Access to Epinephrine Map*, FOOD ALLERGY RES. & EDUC. https://www.foodallergy.org/advocacy/epinephrine/map (last updated July 6, 2016).

[72] *Id.* Hawaii is the only state that does not require or allow schools to stock epinephrine.

[73] Koons & Langreth, *supra* note 68.

[74] *See* Aimee Nienstadt, *Comment, The Insufficiency of the Law Surrounding Food Allergies*, 36 PACE L. REV. 595, 611 (2016) (providing analysis on state epinephrine autoinjector laws). For a discussion of Mylan's role in the enactment of the 2013 Act, see Carrier & Minniti, *supra* note 47, at 67-68.

[75] Ike Swetlitz & Ed Silverman, *Mylan May Have Violated Antitrust Law in its EpiPen Sales to Schools, Legal Experts Say*, STAT, Aug. 25, 2016, https://www.statnews.com/2016/08/25/mylan-antitrust-epipen-schools/ (noting that the "discounted price was $112.10," roughly "a quarter of the cost charged to pharmacies at the time").

[76] *Id.*

[77] *Id.*

[78] Full House Comm. on Oversight & Gov't Reform, *Hearing on Reviewing the Rising Price of EpiPens* (Sept. 21, 2016), *available at* https://www.govinfo.gov/content/pkg/CHRG-114hhrg24914/pdf/CHRG-114hhrg24914.pdf (pt. 1, at 1:44:00) (in testimony to House Committee, Bresch responded to Representative Duckworth's question about whether "schools purchasing discounted EpiPens had to make any representations or warranties to Mylan that they would adhere to certain conditions in order to access the discount price by conceding: 'For people that wanted to buy it at the discounted rate, yes'").

[79] XI HERBERT HOVENKAMP, ANTITRUST LAW: AN ANALYSIS OF ANTITRUST PRINCIPLES AND THEIR APPLICATION ¶ 1807b, at 133 (3d ed. 2006).

a competitor" where there is an adverse effect on competition.[80] Exclusive dealing also can constitute monopolization under Section 2 of the Sherman Act if the defendant has monopoly power.[81] The general concern with exclusive dealing arrangements is that they block competitors from the market and result in higher prices and lower output.

While it is unclear exactly how much of the market was foreclosed by these agreements, antitrust concern is presented by high entry barriers in the form of FDA approval (exacerbated by the agency's caution given potentially fatal consequences from misapplication) and a 400% surge from 15 price hikes between 2009 and 2016.

III. DARAPRIM: RESTRICTED DISTRIBUTION SYSTEM

A final type of behavior is revealed by Daraprim. This drug received attention for its 5000% price increase. But that increase was possible only because of the earlier restriction of its distribution system.

A. Background

Notorious pharmaceutical entrepreneur Martin Shkreli made worldwide headlines in 2015. As CEO of Turing Pharmaceuticals, Shkreli obtained U.S. marketing rights to pyrimethamine (Daraprim) and quickly increased the price 5000%, from $13.50 to $750 per pill.[82] Pyrimethamine is a decades-old drug used primarily to treat toxoplasmosis, a fatal parasitic brain infection that usually occurs in patients with weakened immune systems, such as those with end-stage HIV infection.[83] At the time of the price increase, there were no patents or other forms of market exclusivity.

In addition to increasing price, Turing initiated another less widely understood move—it changed the distribution scheme for the drug. Before its acquisition by Turing, pyrimethamine was available without restriction to patients seeking to fill prescriptions at local pharmacies and to hospitals seeking to stock the product for inpatient use. But in the months before the price hike, apparently as a condition of the sale to Turing, pyrimethamine was switched to a controlled distribution system called Daraprim Direct, in which prescriptions or supplies of the product

[80] 15 U.S.C. § 14 (2012); *see id.*
[81] 15 U.S.C. § 2.
[82] Andrew Pollack, *Drug Goes From $13.50 a Tablet to $750, Overnight*, N.Y. TIMES, Sept. 21, 2015, at B1.
[83] Sara Fazio, Toxoplasmosis, NEW ENG. J. MED. BLOG (Feb. 23, 2012), https://web.archive.org/web/20120422103725/https://blogs.nejm.org/now/index.php/toxoplasmosis/2012/02/23/.

could be obtained only from a single source: Walgreen's Specialty Pharmacy.[84] As a result, hospitals could no longer obtain the drug from a general wholesaler, and patients could no longer find it at a local pharmacy.

Instead, Turing required institutions and individuals to set up accounts through Daraprim Direct, and outpatients were only able to receive the drug by mail order.[85] Comments from Turing executives suggested that a primary goal of the Daraprim Direct system was to make it impossible for anyone other than registered clients to obtain the drug, including generic manufacturers wishing to obtain samples for use in bioequivalence studies needed to obtain FDA approval. This behavior could demonstrate monopolization, with the next two sections analyzing evidence of monopoly power and exclusionary conduct.

B. Monopoly power

Monopoly power has been defined as "the power to control prices or exclude competition."[86] It can be shown in one of two ways, each of which appeared to be satisfied in the case of Daraprim. First, monopoly power can be proved indirectly by examining a defendant's market share along with barriers to entry that could entrench that market position.[87] Courts regularly hold that a 90% market share supports market power, with several courts finding a 75% share to be sufficient.[88]

Evidence that Turing has 100% of the relevant market is provided by the lack of effective, FDA-approved substitutes. Pyrimethamine is part of all widely accepted first-line therapeutic regimens for toxoplasmosis.[89] In fact, the American Society of Microbiology warned that the 5000% price increase would "negatively impact both health care costs and individual patient treatments."[90] Regulatory barriers to entry cement the effect of this high market share as generics can enter the U.S. market only after receiving FDA approval.

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[84] Andrew Pollack & Julie Creswell, *The Mercurial Man Behind the Drug Price Increase that Went Viral*, N.Y. TIMES, Sept. 23, 2015, at B1.

[85] Monica V. Mahoney, *New Pyrimethamine Dispensing Program: What Pharmacists Should Know*, PHARM. TIMES (July 17, 2015), https://www.pharmacytimes.com/contributor/monica-v-golik-mahoney-pharmd-bcps-aq-id/2015/07/new-pyrimethamine-dispensing-program-what-pharmacists-should-know.

[86] United States v. E.I. duPont de Nemours & Co., 351 U.S. 377, 391 (1956).

[87] HERBERT HOVENKAMP, FEDERAL ANTITRUST POLICY: THE LAW OF COMPETITION AND ITS PRACTICE ¶ 6.2b, at 359-60 (5th ed. 2016).

[88] *Id.* ¶ 6.2a, at 357.

[89] Fazio, *supra* note 83.

[90] Memorandum from the Democratic Staff to Democratic Members of the Full House Comm. on Oversight and Gov't Relations, at 5 (Feb. 2, 2016), https://democrats-oversight.house.gov/sites/democrats.oversight.house.gov/files/documents/Memo%20on%20Turing%20Documents.pdf.

Second, monopoly power can be proved directly,[91] such as through observable effects on the market, for example, a price increase or output reduction.[92] Turing's conduct revealed both types of direct evidence.

To begin, Turing significantly increased price. Even though there was not an increase in the costs of producing pyrimethamine (which costs pennies per pill to manufacture[93]), Turing increased the price 5000%. In addition, it was able to maintain this increase despite public outrage and substantial attention from the press and politicians.[94] Given the barriers to entry imposed by obtaining FDA review, the high prices likely will be maintained for an extended period of time.[95]

Output reductions are another direct indicator of monopoly power. After pyrimethamine's price increase, hospitals complained that they were not able to obtain the drug,[96] with Turing's own press release conceding that hospitals and clinics "were having trouble accessing the product."[97]

In short, Turing appears to have monopoly power in engineering and maintaining a 5000% price increase, preventing hospitals from obtaining pyrimethamine, and ensuring the absence of FDA-approved substitutes for the drug.

C. Exclusionary conduct

To bring a successful monopolization claim, a plaintiff must show not only monopoly power but also exclusionary conduct. Courts often distinguish between the "willful acquisition or maintenance of [monopoly] power" and "growth or development as a consequence of a superior product, business acumen, or historic accident."[98] Such a test is easier to state than apply.

In determining whether Turing's refusal to provide samples constitutes exclusionary conduct, consideration of the regulatory background is

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[91] ABA SECTION OF ANTITRUST LAW, ANTITRUST LAW DEVELOPMENTS 69–70 (7th ed. 2012) (noting that "direct proof has provided the basis for findings of substantial anticompetitive effects in some prominent cases").

[92] Broadcom Corp. v. Qualcomm Inc., 501 F.3d 297, 307 (3d Cir. 2007).

[93] *See* Karthick Arvinth, *Daraprim: Generic Version of Drug Costs Less than £0.07 in India*, INTERNATIONAL BUSINESS TIMES (Sept. 25, 2015), http://www.ibtimes.co.uk/daraprim-like-drug-costs-less-0-07-india-1521144.

[94] Pollack & Creswell, *supra* note 84.

[95] *See, e.g.*, Star Fuel Marts, LLC v. Sam's E., Inc., 362 F.3d 639, 654 (10th Cir. 2004).

[96] Letter from Stephen B. Calderwood & Adaora Adimora to Tom Evegan & Kevin Bernier (Sept. 8, 2015), https://consumerist.com/consumermediallc.files.wordpress.com/2015/09/pyrimethamineletterfinal.pdf.

[97] *Press Release: Important News about Daraprim (pyrimethamine)*, (Sept. 18, 2015), https://web.archive.org/web/20150921232830/http://www.turingpharma.com/media/press-release?headline=important-news-about-daraprim%25c2%25ae-%28pyrimethamine%29.

[98] United States v. Grinnell Corp., 384 U.S. 563, 570-71 (1966).

essential. The Supreme Court in *Verizon Communications v. Trinko*[99] explained that "antitrust analysis must always be attuned to the particular structure and circumstances of the industry at issue."[100] In particular, courts must take "careful account" of "the pervasive federal and state regulation characteristic of the industry," and the analysis must "recognize and reflect the distinctive economic and legal setting of the regulated industry to which it applies."[101]

A central objective of the Hatch-Waxman Act is to encourage generic entry.[102] Congress sought to achieve this goal through several mechanisms, including formalizing the expedited pathway and allowing generics to experiment on brand drugs before the end of the patent term.[103] Most relevant for our purposes, the scheme allows generics to earn abbreviated approvals if they can show that their drugs are bioequivalent to the brand's drug.[104] But this crucial element of competition is possible only if the generic has access to the brand firm's samples.[105] Restricted distribution systems threaten this access.

Most prescription drugs are available through a standard pharmaceutical distribution chain: from manufacturer to wholesaler, then to retail or mail-order pharmacy, and then to consumer.[106] The goal is to distribute the drug as widely as possible, as widespread distribution tends to increase manufacturers' revenues by making drugs available to be prescribed to as many people as possible.

Drugs with limited distribution schemes, by contrast, are not available through standard retail or mail-order pharmacies. Instead, the manufacturer eliminates the wholesaler and distributes the drug only through specialty pharmacies it selects. Funneling sales through one wholesaler gives the manufacturer complete control over the distribution chain,

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[99] 540 U.S. 398 (2004).

[100] *Id.* at 411.

[101] *Id.*

[102] *See, e.g.*, Michael A. Carrier, *Unsettling Drug Patent Settlements: A Framework for Presumptive Illegality*, 108 MICH. L. REV. 37, 41-43 (2009).

[103] *See* 35 U.S.C. § 271(e)(1) (2012); Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661, 669-70 (1990) (allowing experimentation before end of patent term would prevent "unintended distortion" of patent laws that would extend "de facto monopoly"); FTC, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 5 (2002), https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf.

[104] FTC, GENERIC DRUG ENTRY, *supra* note, 103, at 5; Lauren Battaglia, *Risky Conduct with Risk Mitigation Strategies? The Potential Antitrust Issues Associated with REMS*, ANTITRUST HEALTH CARE CHRONICLE 26, 28 (Mar. 2013).

[105] Aaron S. Kesselheim & Jonathan J. Darrow, *Hatch-Waxman Turns 30: Do We Need a Redesigned Approach for the Modern Era?,* 15 YALE J. HEALTH POL'Y L. & ETHICS 293, 340-41 (2015).

[106] Kaiser Family Foundation, Follow the Pill: Understanding the U.S. Commercial Pharmaceutical Supply Chain (2005), http://avalere.com/research/docs/Follow_the_Pill.pdf.

which could block generics from samples they need to conduct bioequivalence studies and reach the market.

Restricting the typically expansive distribution scheme also tends to involve conduct that makes no sense other than stifling generic entry. The no-economic-sense analysis asks whether conduct allegedly maintaining a monopoly by excluding nascent competition "likely would have been profitable if the nascent competition flourished and the monopoly was not maintained."[107] Such conduct provides a simple way to determine whether a company's sole motive is to impair competition. If a firm undertakes conduct that makes no economic sense, then its "anticompetitive intent" can be "unambiguously … inferred."[108]

In the regulatory context, and considering behavior that does not make business sense, the leading monopolization cases foreshadow liability. For example, in *Aspen Skiing Co. v. Aspen Highlands Skiing Corp.*,[109] the owner of three downhill skiing facilities failed to offer a justification for withdrawing from a joint ticketing arrangement with the owner of the only other facility in the area.[110] Just as the Supreme Court found liability where the defendant was "willing to sacrifice short-run benefits and consumer goodwill in exchange for a perceived long-run impact on its smaller rival,"[111] a generic that offers to purchase samples at the full retail price can claim that a brand refuses sales that would have been profitable.

In a second example, *Otter Tail Power Co. v. United States*,[112] the Supreme Court required a company to share electric power transmission with rivals. Similar to the facts in that case, in which the defendant was able to "sell [power] at wholesale to those towns that wanted municipal plants" but refused to sell "solely to prevent municipal power systems from eroding its monopolistic position," the brand in this context already is voluntarily selling the drug but restricting its distribution system so that it does not need to sell to others.[113]

The 2015 switch of pyrimethamine to a restricted distribution scheme as a condition of its sale to Turing threatened to result in fewer sales. Drug manufacturers typically have expansive distribution systems. Absent medical necessity, there is no reason to voluntarily restrict

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[107] Gregory J. Werden, *Identifying Exclusionary Conduct Under Section 2: The "No Economic Sense" Test*, 73 ANTITRUST L.J. 413, 415 (2006).
[108] A. Douglas Melamed, *Exclusive Dealing Agreements and Other Exclusionary Conduct—Are There Unifying Principles?*, 73 ANTITRUST L.J. 375, 393 (2006).
[109] 472 U.S. 585 (1985).
[110] *Id.*
[111] *Id.* at 610-11.
[112] 410 U.S. 366 (1973).
[113] *Id.* at 378.

these systems. In this case in particular, with no recent safety concerns, there was no apparent rationale for limiting distribution 62 years after FDA approval.

If there were any doubt as to the reason for the change in the distribution system, it was dispelled by Turing itself. Jon Haas, the director of patient access, admitted that he "would block [a] purchase" of pyrimethamine if a generic sought to order the pill and conceded that Turing "would like to do our best to avoid generic competition" and was "certainly not going to make it easier" for the generics.[114] Turing's insistence on behavior that lacks rational business sense provides strong evidence of blocking rivals. This is a powerful illustration of exclusionary conduct that appears to violate the antitrust laws.

IV. CONCLUSION

Drug price hikes are typically accompanied by justifications based on patents or innovation. The three case studies highlighted in this article show that anticompetitive conduct can play a central role as well. Behavior that makes no sense other than by harming a competitor, that undercuts a regulatory regime, or that involves collusive conduct should not be protected. In targeting this behavior, antitrust scrutiny promises to lower drug prices.

[114] Ed Silverman, *How Martin Shkreli Prevents Generic Versions of his Pricey Pill*, PHARMALOT (Oct. 5, 2015), http://pharmalot.com/how-martin-shkreli-prevents-generic-versions-of-his-pricey-pill/.