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Challenges with Defining Pharmaceutical Markets and Potential Remedies to Screen for Industry Consolidation

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Abstract

Context: Dramatic increases in pharmaceutical merger and acquisition (M&A) activity since 2010 suggest we are in the midst of a third wave of industry consolidation.

Methods: The authors reviewed 168 economic, legal, medical, industry, and government sources to examine the effects of consolidation on competition and innovation and to explore how industry attributes complicate M&A regulation in a pharmaceutical context.

Findings: The authors find that, in spite of certain metrics that might argue otherwise, consolidation consistently reduces innovation and harms the public good. They also find that several factors within the pharmaceutical industry impede proper evaluation of proposed mergers. Because consumer choice across substitutes is limited, pharmaceutical markets frustrate conventional methods of defining markets. Volume bargaining in the pharmaceutical supply chain and asset managers' common ownership of pharmaceutical firms further complicate the definitional process. Hence, the Herfindahl-Hirschman Index (HHI), one measure used by the Federal Trade Commission and the Department of Justice to screen for concerning M&A activity, sometimes depends on faulty market definitions and fails to capture the implications of consolidation for future market share.

Conclusions: The authors describe ways to improve how pharmaceutical markets are defined, highlight quantitative alterations to HHI to account for common ownership, and propose areas requiring further research.

Keywords Herfindahl-Hirschman Index, pharmaceutical industry, Federal Trade Commission, consolidation, mergers and acquisitions

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Recent headlines have heralded dramatic increases in pharmaceutical industry consolidation. In 2019, 1,276 pharmaceutical mergers and acquisitions (M&As) closed worldwide with a total value surpassing $411 billion, setting M&A records for the industry in both volume and value (Alvaro, Challener, and Branch 2020). These numbers suggest we are in the midst of a third wave of consolidation. Upon reviewing 168 economic, legal, medical, industry, and government sources, the most critical of which we highlight in this article, we find that consolidation consistently reduces innovation. Studies note a clear drop-off in new molecular entity and new drug approval rates between the mid-1990s and 2010 following the first two waves of consolidation, which both included large horizontal mergers (Cockburn 2004; FDA 2004; Grabowski and Kyle 2008; Ornaghi 2006; PR Newswire 2000; Ravenscraft and Long 2000; Sharma 2018). Although many metrics suggest heightened innovation levels during the third wave—which has been dominated by large companies acquiring startups—the uptick primarily comprises rare disease treatments, not drugs that promise broad social benefits.

Despite M&As having a history of ill effects on competition and innovation, the Federal Trade Commission (FTC) has challenged few M&As in the pharmaceutical industry over the past 10 years (Tyler and Burnett 2021). This circumstance speaks to the difficulty of evaluating and challenging M&A activity in a pharmaceutical context. This article considers two levels at which the pharmaceutical industry poses complications to regulation. First, at a fundamental level, several features of the industry frustrate conventional methods used to define product markets, which typically assume that some products are interchangeable and that markets are independent of one another. But differences in therapeutic efficacy, as well as limitations imposed by health plans, confound the assumption that products are interchangeable, while the role in drug pricing played by negotiations between drug-makers and pharmacy benefit managers (PBMs) confound the assumption that markets are independent. Based on our synthesis of findings from economic and legal literature as well as regulatory agency and court documents, we suggest that these and other industry attributes lead competition authorities to define pharmaceutical markets alternately too narrowly and too broadly.

Imprecise market definitions are not only problematic in the abstract. Market definition is central to calculating market concentration, a metric deployed by the FTC and the Department of Justice (DOJ) to assess whether proposed M&As should be subject to further regulatory review. Indeed, the FTC and DOJ use the Herfindahl-Hirschman Index (HHI), one such measure of market concentration, to set merger guidelines (DOJ and

FTC 2010). Given HHI's influence as a screening tool, its pitfalls constitute a second level of difficulty in M&A regulation. Furthermore, market concentration measures fail to account for effects of consolidation on future innovation and nascent competition.

The insufficiencies of current pharmaceutical market definitions—resulting in inaccurate measures of market concentration—have significant consequences for the regulation of anticompetitive behavior. While engineering precise solutions to these problems falls beyond the scope of this article, we highlight several areas of greatest need and discuss both existing research and potential directions for further study. More specifically, we recommend making quantitative alterations to the HHI formula as well as structural reforms that support more holistic regulatory processes.

Consequences of Consolidation

An examination of merger and acquisition activity in the pharmaceutical industry reveals three discrete waves, each characterized by a marked rise in number of deals and transferred market value within a specific time frame (Grabowski and Kyle 2008: 283; Ravenscraft and Long 2000). The first wave spanned approximately 1989–1990, the second spanned 1994–early 2000s, and the third began around 2010 and is still ongoing (Comanor and Scherer 2013; Gagnon and Volesky 2017: 1; Grabowski and Kyle 2008; Grabowski and Kyle 2012: 553; Ravenscraft and Long 2000: 288–89; Richman et al. 2017: 290–91; Siebert and Tian 2020; Ward 2015). Each wave has permanently shifted the industry toward a more consolidated state. Table 1 assembles the US Census Bureau's data on the market concentration of the pharmaceutical industry, which the bureau collects every five years, over the period encompassing these three waves. Despite a small dip in the 4-firm concentration ratio—the sum of the market shares of the four largest firms in the industry (Kenton 2020)—between 2002 and 2007, the 4-, 8-, and 20-firm concentration ratios otherwise stabilize and/or increase across each of the waves. The higher the concentration ratio, the greater the market share held by the industry's largest firms, and the less competition there is in the industry. The data show that consolidation rates are typically maintained at successively higher plateaus at the end of each wave (see figures for 1992 and 2002 in table 1; Comanor and Scherer 2013: 107).

These trends are similarly visible in the overall structure of the pharmaceutical industry. For example, the eight-firm concentration ratio rose from 36% in 1987 to 58.3% in 2017 (table 1). Dalton and Penn (1976: 140; see also Bain 1951: 293–324) have found that once an industry's eight

Table 1 US Pharmaceutical Industry Concentration Ratio by Year

Year	4-firm ratio	8-firm ratio	20-firm ratio
1987	22.0	36.0	65.0
1992	26.0	42.0	72.0
1997	35.6	50.1	71.4
2002	36.0	53.3	75.8
2007	34.5	54.2	75.9
2012	37.2	53.3	72.3
2017	43.9	58.3	77.1

Notes: Data was compiled from the US Census Bureau's "Manufacturing: Subject Series: Concentration Ratios: Share of Value of Shipments Accounted for by 4, 8, 20, and 50 Largest Companies for Industries" reports for the years 1987, 1992, 1997, 2002, 2007, 2012, and 2017. The industry examined is "pharmaceutical preparation manufacturing" (Standard Industrial Classification Code 2834 [1987–92], North American Industry Classification System Code 325412 [1997–2017]). No analysis has been applied to the data.

largest firms hold 60% or more of the industry's market share, the industry becomes oligopolistic rather than competitive. The 2017 eight-firm concentration ratio approaches this threshold, indicating that the pharmaceutical industry is close to reaching such an oligopolistic state. In addition, M&A transactions, which were once more common among branded firms, have recently become widespread in the generics industry as well (Gagnon and Volesky 2017). There were 42 generic mergers in 2016, up from zero in 1995 (1), and as of 2017 the four largest generics companies produced 50% of all generic drugs sold (Coopman 2017).

Considerable economic debate exists regarding the effect of market structure on innovation. In a pair of contrasting positions commonly referred to as the Schumpeter-Arrow debate, Schumpeter (1994: 106) holds that market concentration promotes innovation, and Arrow (1962: 619) holds the opposite. Shapiro (2012: 378–80) argues that the two views are compatible, finding substantial empirical evidence that more competition spurs firms to be more efficient and to invest more in R&D, but that concentration cannot necessarily serve as a proxy for the intensity of competition. With these varying viewpoints in mind, we look to other evidence of the innovative effects of increased competition in the three waves of pharmaceutical concentration.

The literature overwhelmingly agrees that pharmaceutical innovation decreased following the first two merger waves of 1989–1990 and 1994–early 2000s. Although rates can fluctuate from year to year, studies note a clear drop-off in new molecular entity and new drug approval rates between the mid-1990s and 2010 (Cockburn 2004: 11; FDA 2004; Grabowski and

Kyle 2008; Ornaghi 2006; Ravenscraft and Long 2000; Sharma 2018). The Center for Drug Evaluation and Research, for example, reported approving 53 small-molecule drugs and biologics in 1996 but just 21 in 2010 (Sharma 2018). Furthermore, a study of large mergers between 1988 and 1999 demonstrated that the number of projects under active development declined an average of 34% in the three years following merger consummation (PR Newswire 2000). At the same time, research has become less efficient (Scannell et al. 2012). "Eroom's Law"—a tongue-in-cheek reversal of "Moore's Law," which states that the number of transistors per circuit or microchip doubles every two years—holds that the number of new FDA-approved drugs per billion USD of R&D expenditures has halved every nine years since 1950 (191). Indeed, the decline in drug approvals between 1996 and 2010 overlaps with a tripling of research and development spending across the industry (Cockburn 2004; Gilbert 2020: 126; Mikulic 2021). Even those cautious about raising alarms acknowledge that there are "real grounds for concern" (Cockburn 2006: 25).

One could argue that a correlation between merger waves and decreased innovation does not necessarily mean that increased M&A activity leads to decreased innovation; it is also possible that decreased innovation may prompt M&A activity. For example, drug companies may opt to merge upon realizing that they can no longer "easily" develop new drugs and that merging would constitute a more efficient method of increasing profit. However, Cunningham, Ederer, and Ma (2021) demonstrate that companies have a strong incentive to engage in what they term "killer acquisitions," whereby an incumbent firm acquires an innovating firm for the sole purpose of shutting down its product development to eliminate potential future competition. Cunningham, Ederer, and Ma further show that by a conservative estimate, at least 5.3% to 7.4% of pharmaceutical acquisitions between 1989 and 2010 can be classified as killer acquisitions (20). These results indicate that at least some proportion of pharmaceutical mergers were undertaken with the intent to hamper new drug development. Other research has noted that, intentions aside, consolidation shrinks the horizon for future innovation. Comanor and Scherer (2013: 107–8) argue that progress is best facilitated when different groups using different methods pursue the same goal at the same time, a strategy known as "parallel paths," because having a greater number of experiments in progress can help to compensate for the high degree of uncertainty involved in and the length of time needed for pharmaceutical discovery. Because mergers foreclose parallel paths as research and development arms are consolidated

(Cunningham, Ederer, and Ma 2021; Gilbert 2020: 129–30), they reduce opportunities and increase the time it takes for drugs to be developed. Moreover, the significance of parallel paths suggests that typical metrics such as number of newly approved drugs or number of newly filed patents cannot convey the true impact of consolidation on innovation, because these metrics do not account for how consolidation affects ongoing and future research.

In contrast to the first two waves, the third wave has coincided with a shift in M&A practice and a rise in new molecular entities. Despite appearances to the contrary, the ability of these developments to strangle nascent competition is concerning for competiton and innovation.

The shift in M&A activity plays out in the following manner. While mergers have historically occurred as a matter of established drug companies combining, recent consolidatory activity has been characterized more heavily by large incumbents acquiring startups (Chancellor 2020: 14–15; Comanor and Scherer 2013: 111; Khetan 2020: 42). These acquisitions speak to the growing specialization of pharmaceutical companies in different stages of drug production: large firms focus on navigating the FDA's regulatory process, while startups emphasize high-risk research and early development (Comanor and Scherer 2013: 111; Khetan 2020: 37; Shepherd 2018: 1). Such divergent priorities are reflected in the data. As innovative output concentrates among smaller firms, the top 10 pharmaceutical companies' share of new drug approvals has declined from 52% in 2013 to just 25% in 2018 (Geilinger 2019: 16–17). Meanwhile, smaller pharmaceutical companies—defined as companies with sales of less than $100 million—were responsible for 49% of the drugs approved in 2018 (16).

Because specialization ostensibly puts startups and incumbents in different markets, it may not be obvious how acquisitions can be harmful. After all, occupants of different markets do not compete directly with one another, so acquisitions would not pose a risk of oligopoly. Furthermore, as Gilbert (2020: 130) rightfully makes clear, acquisitions of startups by large companies are not intrinsically negative; the prospect of acquisition can help to incentivize the formation of startups and the initiation of new R&D projects. But an overly optimistic view of such acquisitions fails to take into account the fact that pharmaceutical startups can also be classified as nascent competitors. That is, though they may not compete with incumbent firms at the moment, they have the potential to become competitors given sufficient time to grow (Gilbert 2020: 130; Hemphill and Wu 2020: 1880–81). Today's startup has the potential to be tomorrow's

Genentech—that is, a large, major competitor in the field. An ecosystem in which potential competitors are routinely purchased and absorbed when they are in the cradle raises competition concerns.

Moreover, startups perceived as threatening—and the drug products they are in the process of developing—are at particular risk of being snuffed out by incumbents in killer acquisitions (Gilbert 2020: 130). The possibility is all the more concerning given that the size differential between startups and incumbents allows acquisitions more readily to bypass regulatory scrutiny (Cunningham, Ederer, and Ma 2021: 33–35). A big fish buying a single small fish seems unlikely to trigger regulatory warning signals about the additional power of the big fish. Additionally, as was true of the first two merger waves, consolidation better enables firms to suppress competitors with the aid of PBMs (Feldman 1999; Feldman 2019: 22). These circumstances, further detailed later in this article, establish that incumbent acquisitions of startups do in fact have consequences for competition and innovation.

Similarly, although the rise in new drug approvals suggests improved R&D activity, the characteristics of these drugs raise other concerns not captured by strictly quantitative metrics. Most drugs released during the third wave have been rare disease treatments. In 2018, 34 of 59 new molecular entities received the "orphan drug" designation (FDA 2019: 10) granted to therapies addressing diseases affecting fewer than 200,000 people (FDA n.d.). Compare this with 2008, when just five of 21 new molecular entities were considered orphan drugs (Hughes 2009: 95). One report calculates that the percentage of orphan drugs among newly launched drugs increased from 10% to 44%—a more than fourfold increase—between 1998 and 2017 (AHIP 2019: 1). Insofar as these drugs actually do serve small populations, they are unquestionably valuable for the patients they serve, but the sharp shift may speak to an incentive structure that directs attention toward rare diseases while leaving areas that are less lucrative—but have a broader reach—wanting (Feldman 2020b). When the majority of the nation's innovation focus shifts to treatments for small populations, research on treatments for disease states that affect large populations may languish.

Some commentators suggest that the shift to orphan drugs reflects, in part, an attempt to capture orphan benefits for treatments aimed at larger groups; for example, by shifting toward populations, such as cancer patients, that can be sliced into small subgroups to obtain numerous orphan protections (Chua, Kimmel, and Conti 2021; Daniel et al. 2016; Tribble and Lupkin 2017). To the extent that this is correct, the shift again represents

a distortion in innovation. It may also have potential implications for increased consumer prices from strategic gaming (Daniel et al. 2016: 211). Orphan drugs command annual prices that are, on average, 25 times higher than those of traditional drugs (AHIP 2019: 3), enjoy an additional seven years of marketing exclusivity (FDA n.d.; AHIP 2019: 2), and frequently receive priority reviews from the FDA (Miller and Lanthier 2018: 4), which also permits them to have smaller trials, lowering their phase III clinical trial costs (Khaleel n.d.). The shift toward orphan drugs consequently improves therapeutic access for the few to the detriment of the many.

In addition, a consolidated sector of the pharmaceutical industry that controls the process of FDA approval could leave new innovators with little recourse other than acquisition or partnership with an entrenched firm, prompting antitrust concerns (Richman et al. 2017: 787). Public regulation of drug development stems from a desire to protect patients. Secondary gatekeeping by pharmaceutical companies does not.

Characteristics of Pharmaceutical Markets

Despite the demonstrably problematic results of consolidation, M&As in the pharmaceutical industry are difficult to evaluate. Constraints on consumer choice and the prevalence of volume bargaining render drug products alternately noninterchangeable and mutually dependent, leading market boundaries to shift in different contexts. As a result, it is challenging to come up with precise market definitions, a circumstance that poses a fundamental problem to quantitative evaluations of competition in pharmaceutical markets.

Patients differ from most consumers in that even drugs developed to treat identical ailments are not consistently interchangeable. This fact contravenes conventional methods of determining market definition, for which product interchangeability is a central tenet (Brown Shoe Co. v. United States 370 U.S. 294 [1962]). Consider the "hypothetical monopolist" test, "one of the organizing principles" of the FTC and DOJ's Horizontal Merger Guidelines (Harkrider 2015). This test evaluates whether a market has been properly defined by determining whether a monopoly firm in the proposed market would make or lose money if it made a "small but significant nontransitory increase in price" (SSNIP) (DOJ and FTC 2010). If the SSNIP is not profitable, the closest substitute product is added to the proposed market, and the test is repeated. This process continues until the SSNIP becomes profitable for the monopoly firm. At this point, the market is considered appropriately defined.

This method of generating market definition assumes that consumers change their purchasing habits in response to changes in pricing. But when it comes to pharmaceuticals, consumer choice is limited by numerous attributes particular to the drug product and to the patient using it. Comorbidities, pregnancy, sex, age, interactions with other medications, and other factors may generate contraindications that bar a patient from certain drugs. A drug that is not outright unsafe may nevertheless be less therapeutically effective or may produce less tolerable side effects than a cognate medication. This can be true even of a brand-name drug and its biologically identical generic equivalent (Neighmond 2020). In short, unlike most consumer products, no two drugs are by default interchangeable just because they perform the same therapeutic function.

Consumer choice is also restricted by the way in which drugs are accessed and sold (Demperio and Fauver 2017). Consumers gain access to prescription drugs only by receiving a prescription from a physician, meaning that they are not at liberty to shop alternatives without physician input. Indeed, a physician may continue to prescribe an expensive brand version of a drug over a generic or cheaper competitor if the brand is working well (Davari, Khorasani, and Tigabu 2018). At the same time, some state pharmaceutical laws require that pharmacies automatically substitute brand-name small-molecule drugs with available generic alternatives (though this does not happen for biosimilars) (Cauchi 2019), which physicians can override with a notation not to substitute. Health plans add another layer to this process with formularies, which they use to organize the prescription medications they cover. Formularies feature different tiers of medications that carry different copays, with higher tiers associated with higher copays. Health plans place drugs on lower tiers to incentivize patients to select them over similar drugs on higher tiers (Feldman 2021). But tier placement can raise concerns, and some plans place the cheaper version of a drug with the same active ingredient on the same or a less advantageous (i.e., higher) tier than the more expensive brand (Feldman 2021). Mis-tiering not only causes patients to spend more but also limits patients' abilities to substitute even biologically identical drug products for one another. Coupled with the facts that not every health plan covers every drug (Gill 2020) and that prices for prescription drugs can vary significantly across states and zip codes because of differences in pharmacies, payors, and other factors (Kullgren et al. 2017), formulary placement can further impede interchangeability of drug products.

If therapeutic effects and consumer access explain why pharmaceutical product markets must be narrowly defined in some cases, volume

bargaining explains why those same markets should be analyzed in concert with one another in other cases. The prevalence of volume bargaining in the pharmaceutical industry can be attributed to the prominent role played by PBMs, who negotiate prices with pharmaceutical companies on behalf of health plans and are responsible for providing the plans with treatments covering any number of medical conditions (Feldman 2020a; Feldman 2021). These negotiations provide pharmaceutical firms with the opportunity to offer discounts on the basis of quantity of products purchased, also known as "volume rebates." To be clear, the line between procompetitive and anticompetitive forms of collaboration can be thin (Greaney 1995), and volume rebates can be procompetitive depending on the context in a particular industry (Feldman 2019: 28). When it comes to pharmaceuticals, rebates can be procompetitive if they lead to circumstances in which the patient pays less for the drug and pays a lower health plan premium in both the short term and the long term. In fact, PBMs were integrated into the pharmaceutical supply chain with procompetitive ends in mind: the larger the discount off the list price a PBM negotiates, the more it gets paid by the health plan for which it acted (Feldman 2020a: 326–27). Because PBMs may keep all or part of the rebates, however, this process incentivizes PBMs and pharmaceutical companies to work together to squeeze out more profit, often at the literal cost of patients (Feldman 2020a). More insidiously, pharmaceutical companies can amass volume and breadth of products without ringing any antitrust alarm bells.

For example, a firm controlling 20% of the thrombolytic agent market is unlikely to attract excessive regulatory attention because its market share is within levels deemed reasonable by regulatory authorities (DOJ and FTC 2010). By acquiring similar shares of many other markets, such as cancer treatments, topical anesthetics, and antiemetic agents, the firm can avoid triggering regulatory review in any single market while nevertheless controlling a massive volume of drug supply. The firm can then leverage its varied holdings in negotiations through PBMs by offering volume rebates (Feldman 2019: 21–25). In one version of this offer, the firm promises the PBM its lowest price per unit for each of several drugs within a package as long as the buyer purchases a sufficient quantity of every drug in the package (Feldman 1999: 2104–5; Feldman 2019: 21–25). Because PBMs facilitate the purchase of drugs across multiple markets, the firm's distributed presence becomes a monopolistic advantage. A potential competitor may be able to match the rebated price of one drug in the package, but without shares in other drug markets, the single reduction is insufficient to draw clients away (Feldman 1999: 2104–5; Feldman 2019: 21–25; SmithKline

Corp. v. Eli Lilly & Co., 427 F. Supp. 1089 [E.D. Pa. 1976]). To the extent that an incumbent firm's acquired startups make a range of drug products, the PBM issue would remain salient even in the case of third-wave acquisitions.

Pharmaceutical companies can combine volume rebating with the limitations set by the patent system to further their advantage. If the firm offering a volume rebate holds unexpired patents on one or more drugs in its package, it essentially bars other firms from offering competitive packages because those patented drugs lack generic equivalents. A competitor would be unable to offer a package that covers the conditions treated by those drugs (Feldman 2020a: 330–31). As a result, merely by virtue of bundling with an unrelated protected drug, any unprotected drugs in the firm's package can become privileged by the health plan over cheaper alternatives. Indeed, pharmaceutical companies have used this method to protect the market share of drugs that have recently become or will soon become vulnerable to competition from generic equivalents (332–35). Mergers between a firm with patented holdings in some markets and companies that control shares in other markets may not appear to increase concentration in any particular market—after all, a patented market has only one drug in it to begin with—but can have impacts across markets. Similarly, a new entrant trying to break into the market could be unable to gain traction. Some state laws provide that patients may remain on a particular version of a drug in certain circumstances. When the rebate package includes specialty drugs priced at hundreds of thousands of dollars a year, a smaller health plan would be loath to turn down the brand's rebate offer. Given that some patients will remain on the high-priced version, which the health plan must now purchase without the rebate, the new entrant must provide a rebate that compensates for the health plan's lost offer from the brand. Coupled with the exclusivity periods provided by an orphan drug designation, drug companies' efforts to retain revenue with the aid of the patent system can have devastating consequences for patients.

In these ways, pharmaceutical companies can use volume rebates to prevent even less-expensive challengers from gaining a competitive foothold (Feldman 2021). Mergers compound this effect even when they appear to increase only the breadth and not the depth of market-based power, because the broader a firm's portfolio, the more drugs it can bundle together (Dunn 2019; Feldman 1999: 2103–5; Feldman 2021: 15–16). In short, as a result of the role of PBMs in the pharmaceutical industry, pharmaceutical product markets cannot always be considered fully independent

from one another with respect to bargaining power. Recent cases challenging anticompetitive behavior on the basis of bundled pricing under section 1 or 2 of the Sherman Act have held that plaintiffs have a high burden of proof (Cascade Health Sols. v. PeaceHealth, 502 F. 3d 895 [9th Cir. 2007]; John Doe 1 v. Abbott Laboratories, 571 F. 3d 930 [9th Cir. 2009]; Eisai, Inc., v. Sanofi Aventis US, LLC 821 F. 3d 394 [3rd Cir. 2016]). Given this fact, prophylactic measures such as merger enforcement are all the more important.

The potential harm that can be caused by inappropriate market definitions is not just theoretical. Similar problems around market definition arose with respect to "innovation markets" in the mid-1990s. While the 1995 *Antitrust Guidelines for the Licensing of Intellectual Property* relied on "the capability to engage in R&D" as a measure of innovation, the relationship between R&D and innovative output was too obscure to define an innovation market (Aziz 1995). These difficulties in defining innovation markets made it difficult to analyze the true competition effects of mergers in such markets. Pharmaceutical companies themselves recognize the power of market definition in antitrust evaluation, a fact made evident by the lengths to which companies go to broaden market boundaries. In *SmithKline Corp. v. Eli Lilly & Co.* ([3d Cir. 1978] 575 F.2d 1056), for example, Lilly attempted to ward off an antitrust challenge to its monopolization of the cephalosporin antibiotic market by arguing that the relevant market should include *all* antibiotics. Though the court rejected the argument on the grounds that not all antibiotics are therapeutically substitutable (1065), Lilly's efforts suggest how influential market definitions can be for regulatory oversight. In the following section, we consider how difficulties defining pharmaceutical markets play out in a regulatory context with respect to HHI, a measure of market concentration that relies on accurate market definition for its calculation.

Problems with the Use of HHI When Markets Are Inappropriately Defined

HHI is a standard gauge of market concentration used by the FTC and the DOJ to assess consolidatory activity. HHI is measured by the sum of the squares of the market share occupied by each competing firm and can range from close to zero (reflecting a highly fragmented market) to 10,000 (reflecting a perfect monopoly) (DOJ 2018). When a merger or acquisition is proposed, the FTC assesses its potential harm to competition by calculating the HHI value of the relevant market before the merger takes

place and the HHI value of the same market after the merger takes place (DOJ and FTC 2010). If the postmerger HHI value and/or the magnitude of the increase in HHI following the merger exceed certain thresholds, further regulatory review is triggered; if not, the merger or acquisition is generally permitted to pass without inquiry. These threshold values are uniformly applied across industries.

Given that the FTC has finite resources, its reliance on HHI and on standardized thresholds to triage M&A activity is understandable. Nevertheless, the centrality of HHI to merger assessment has had unintended consequences for the interpretation and use of the measure. Market definition poses a particular challenge to the regulatory use of HHI in a pharmaceutical context. Because HHI is calculated per product market, it—like other measures of market concentration, such as concentration ratio—is only useful so long as the market is appropriately defined. That is, if the market for which a concentration is being calculated does not accurately represent the effects of competition on the included products, the calculation will fail to warn consistently against antitrust concerns in that market. The DOJ and FTC recognize this danger, noting in their 2010 Horizontal Merger Guidelines that both overly broad and overly narrow market definitions "can lead to misleading market shares" (DOJ and FTC 2010: 8). Nevertheless, the agencies continue to depend primarily on the hypothetical monopolist test to identify markets by product and geographic region (8–15). As we demonstrated earlier in the article, however, the hypothetical monopolist test, like other methods of market definition that rely on product interchangeability, elides significant features of the pharmaceutical industry. Folding such faulty market definitions into HHI kneecaps its utility in regulating pharmaceutical M&As.

Market definition is not the only concerning aspect of regulatory dependence on HHI. Despite the FTC's insistence that "the purpose of these thresholds is not to provide a rigid screen to separate competitively benign mergers from anticompetitive ones" (DOJ and FTC 2010), companies and regulators alike treat deals whose perceived effects on HHI are low as nonthreatening. It should come as no surprise that changes to FTC guidelines involving HHI also influence perceptions of which kinds of M&As are permissible. This consequence came to pass in 2010. Before that year, the FTC's Horizontal Merger Guidelines stated that a postmerger HHI of 1,800 and an increase of 100 points or more likely indicated unacceptably high market concentration (DOJ and FTC 1997). But as concentration levels surged in several industries during the 1990s and 2000s (Hamilton Project 2018), the FTC began to appear increasingly ineffectual as

threshold-exceeding mergers proceeded without challenge. Meanwhile, market participants were left without clear expectations as to whether the agency would intervene in any given merger. The FTC finally decided to raise the thresholds in 2010, citing the need to conserve enforcement resources for the most problematic cases. Under the new guidelines, a postmerger HHI of 2,500 (corresponding to a market divided evenly among four firms) and an increase of 200 points or more is needed to prompt further review (DOJ and FTC 2010).

Unfortunately, this adjustment proved counterproductive. Far from improving the FTC's capacity to protect against anticompetitive behavior, the raised thresholds legitimized a new normal for market concentration. Industry leaders "unsurprisingly interpreted the change in policy as reflecting a greater tolerance for concentration," which "ratchet[ed] up the egregiousness of the mergers being considered" (Abdela and Steinbaum 2018: 4). One would not want to overstate the extent to which the new threshold affects merger challenges. As Shapiro and Shelanski (2021) find, in the 10 years before and after the 2010 change, agencies rarely challenged mergers that resulted in an HHI close to the threshold level. Nevertheless, the cases that end up in court are only part of the challenge process, with the agencies settling cases far more frequently than they pursue litigation (Shapiro and Shelanski 2021). Thus, the greatest impact of HHI may involve its use as a screening tool to identify potential mergers for which the agency requests additional information from companies. Given that the threshold signals the boundary between what is acceptable and what is not, changing that boundary may mean that levels of anticompetitive behavior, market control, and patient exploitation currently considered unreasonable can become unremarkable over time as limited resources lead regulatory bodies to continue redrawing the lines.

Beyond such hermeneutic challenges, the FTC's use of a uniform threshold value across all industries is problematic. As Roberts (2014), Smith and Ocampo (2021), and Benkard, Yurukoglu, and Zhang (2021), among numerous others, have demonstrated, different markets have different characteristics, making levels of concentration that are appropriate for one industry inimical to consumer and market welfare in another. In a pharmaceutical context, high levels of concentration can be particularly damaging. Generic drug pricing, for example, inversely correlates to the number of manufacturers, dropping from a median of 61% of brand-name average price for a generic with one seller to just 1% with 10 or more sellers (Conrad and Lutter 2019: 9). Accordingly, reduced competition between pharmaceutical companies affects not only the kinds of drug products available to patients for purchase but also the amount that patients must pay

to maintain their health. Furthermore, as described in the previous section, patients, unlike consumers of most other goods, typically have more difficulty altering their purchasing activity in response to pricing. If lack of competition prompts pharmaceutical companies to hike up the cost of their products, lives can be left hanging in the balance. The post-2010 HHI threshold of 2,500 may therefore inadequately protect consumers' access to critical medicines.

Finally, regulatory dependence on HHI incorporates blind spots into M&A evaluations that are inherent to HHI itself. For example, the literature raises concerns over the difficulty for regulators of evaluating pharmaceutical markets to account for the competitive implications of common ownership, to distinguish between competitive and anticompetitive mergers, and to assess merger impact on future market shares. To the first point, recent studies show that different brand pharmaceutical companies—that is, pharmaceutical companies with R&D capabilities—share many of the same large institutional investors (Banal-Estañol, Newham, and Seldeslachts 2021). These investors, which include powerful investment groups such as Blackrock, Vanguard, and Fidelity, can and do influence the strategic decision-making of companies in which they have holdings (73–74). Elhauge (2016) has shown that common shareholdings diminish incentives for firms in the same industry to compete against one another. In traditional markets, competing firms engage in price-undercutting to capture market share from one another (Elhauge 2016). When there is an overlap in firm ownership, firms have a weakened incentive to undercut prices, because this practice hurts shareholder profits for all (Elhauge 2016). Common ownership can, therefore, exacerbate anticompetitive behavior and magnify the effective market concentrations of firms with overlapping owners (Azar, Schmalz, and Tecu 2018). Similar problems are at work when firms share common private equity investors, a growing trend in the health care industry (Scheffler, Alexander, and Godwin 2021: 45–49). Others have expressed concerns over the difficulties of capturing these issues in quantifiable terms that regulators can easily apply (Phillips 2018) as well as the importance of analyzing common ownership in the context of industry structure and incentives (Patel 2018). Yet, because of the lack of common-ownership data, market concentration measures such as HHI, at least as it is applied in a regulatory context, do not capture the consequences of common ownership for market share (Azar, Schmalz, and Tecu 2018), enabling behavior that should elicit a closer look to fly under the radar.

Evaluating M&As is a complex process that includes evaluating the change and the resultant market concentration as well as other factors

that could dampen anticompetitive concerns such as consolidation-specific efficiencies, ease of entry, and the market power of buyers. Competitive mergers and future market shares are two additional, and related, nuances that fall beyond the scope of a market concentration–based evaluation, with particular implications for the ongoing third merger wave. As noted earlier, it can be difficult to assess whether a large incumbent's acquisition of a small startup is anticompetitive because of their differing functions and sizes. On the one hand, if large incumbents and small startups are assessed as firms in the same market, acquisitions of small startups by large incumbents can slip regulatory notice because startups tend to have low enough market share that the change in HHI can easily fall below threshold values that warrant concern and scrutiny. When market share is the only metric under consideration, acquisitions made in good faith with procompetitive promise register identically to killer acquisitions. On the other hand, if incumbents and startups are assessed as members of different markets as a result of the pharmaceutical industry's increasing specialization, such "cross-market" acquisitions would not even induce HHI calculation.

Even if regulators were able to distinguish between procompetitive and anticompetitive mergers at the moment of the merger, they might be incapable of reckoning with competitive potential. As nascent competitors, any startup can become capable of challenging incumbent firms, not only by developing novel drug products that compete with existing treatments but also by developing familiarity with regulatory pathways and relationships with regulators commensurate with those of incumbents. Put differently, if one major barrier to competition between startups and incumbents lies in the fluency of the incumbents in navigating the drug approval process, then if startups develop such fluency, that would enable the parties to compete. And because such fluency is a function of experience, acquisitions that enfold startups into larger companies before the startups have the time or opportunity to gain such experience may stifle future competition (Feldman 1999), even if the acquisitions are made without anticompetitive intent. As a measure of market concentration at a single moment in time—the moment that the merger deal is proposed—market concentration measures such as HHI do not capture such a long view of risk to competition.

The problem is not exclusive to incumbent acquisitions of startups. Just as HHI cannot account for the consequences of experience for future competition, the measure similarly cannot account for the effects of present research efforts on future market share. It therefore inadequately captures the harm certain M&A proposals may pose to drug development in the long run. Take as an example the massive Ciba-Geigy-Sandoz merger that

created Novartis. In the FTC's review, regulators had to rely on indirect methods to determine that although no gene therapies had yet been introduced to market, both merging companies were so dominant in gene therapy research that the postmerger entity would leave little to no competition in that domain (Meier, Albert, and Brau 2013: 114). So long as the FTC relies on HHI to trigger merger reviews, M&A activity of less prominence than the Ciba-Geigy-Sandoz merger may escape regulatory attention, with the result that such indirect measures will never be applied. This deficit in regulatory review creates potentially damaging consequences for innovation and future competition.

Proposed Solutions

In light of the problems highlighted above, several potential alterations could provide improvements. The first concerns market definitions and has particular implications for pharmaceutical regulation as a result of patients' lack of flexibility in purchasing decisions. Present market boundaries run the gamut from the American pharmaceutical industry as a whole (Richman et al. 2017: 795) to highly specific products such as fluocinolone acetonide 0.01% solution (Dave et al. 2017: 4). Better boundaries would take into account the therapeutic effects of different drugs, their geographic and economic accessibility to patients, and the strength of consumer preferences. These categories would, in turn, prompt regulators to consider related factors: economic accessibility may depend on variable coverage by insurers, while consumer preferences may be colored by side effects or variations in efficacy.

Quantitative alterations may tackle the competitive disparity between small and large firms and the problem of common ownership. As described earlier, smaller firms' dependence on larger ones for the resources to navigate FDA approval means that a merger between small firms may be procompetitive rather than anticompetitive. To account for this possibility, Anbarci and Katzman (2015) suggest that mergers involving purely the smallest firms should be viewed as procompetitive, reflecting the postmerger entity's greater ability to compete with established firms. Meanwhile, the Modified Herfindahl-Hirschman Index (MHHI), which defines market concentration as comprising both industry concentration and common ownership concentration, may help address the problem of common ownership (Azar, Schmalz, and Tecu 2018; Bresnahan and Salop 1986). Although some industry experts have suggested that even the MHHI falls short of fully capturing the nuances of common ownership (Florian & Gron

2019), its use in place of or in addition to HHI, particularly if more finely tuned, could better alert regulators to the risk of anticompetitive behavior.

Market definition and quantitative alterations cannot correct all of HHI's blind spots. Others are better remedied by using complementary metrics. Most crucially, competition authorities should develop a measure that can account for the bundling of drugs and volume bargaining power exerted by pharmaceutical companies with widely distributed market presences in negotiations with PBMs. While it may be difficult or impossible to break apart a merger after research labs and other facilities become integrated, postmerger review would, at the very least, serve as an opportunity to educate enforcers and courts about the market conditions likely to be problematic. This would enable them to better spot these conditions in the future and to direct regulatory attention accordingly.

Finally, Congress and competition authorities must reevaluate the decisions that have produced the current circumstances. The 2010 update to the Horizontal Merger Guidelines, at least partially a response to a lack of regulatory capacity, made room for the pharmaceutical industry's appetite for consolidation. That guideline change should be reevaluated. Similarly, for the FTC to do its job properly, the agency needs Congress to appropriate sufficient resources as well as support from sister agencies, such as the DOJ and state and international competition authorities. Furthermore, rather than relying on crystal-ball predictions, competition agencies should establish a system of postmerger review to ensure past decisions had the intended results and to improve future evaluations. The FTC's recently announced Multilateral Working Group may serve as one forum in which to address the role of government regulation of pharmaceutical mergers on an international level.

Conclusion

Consolidation in the pharmaceutical industry has historically reduced innovation, and the current wave of M&A activity continues to raise concerns. We find that, in spite of certain metrics that might argue otherwise, consolidation consistently reduces innovation and harms the public good. We also find that several factors within the pharmaceutical industry impede proper evaluation of proposed mergers. Because pharmaceutical drugs are only offered to consumers via a prescription whose coverage is determined by an insurer, consumer choice across substitutes is limited, frustrating conventional methods of defining markets. Market definition is further complicated by volume bargaining in the pharmaceutical supply chain and common ownership of pharmaceutical firms by asset managers.

Hence, HHI sometimes depends on faulty market definitions and fails to capture the implications of consolidation for future market share. We describe ways to improve how pharmaceutical markets are defined given restricted consumer choice and volume bargaining, suggest quantitative alterations to the HHI to account for common ownership, and propose areas requiring further research that can account for these nuances and mediate regulatory weaknesses.

■ ■ ■

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