

Competition and Antitrust Issues in the Pharmaceutical Industry

FINAL REPORT

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Table of Contents

I. Introduction and Overview	3
II. Economic and Policy Background	4
1. The Originator Pharmaceutical Sector	4
R&D, patents and exclusivities	4
Regulation of Market Entry: Safety, Efficacy, Quality; Promotion.....	6
Insurance coverage and price regulation.....	6
Physician Agency	8
2. Generics	8
Market Access Regulation of Generics.....	9
Reimbursement of Generics	11
3. Retail Pharmacies.....	12
4. Pharmaceutical Markets in Middle and Low Income Countries (MLICs)	13
Originator drugs	13
Generics	15
Retail Pharmacies.....	16
III. Types of Antitrust Cases in the Pharmaceutical Industry	19
1. Monopoly and monopolization.....	19
Mergers and Acquisitions, and Licensing Deals	19
Patent evergreening and product switching.....	19
2. Agreements on price	20
Price Discrimination	20
3. Agreements not to compete: Pay-for-delay (“reverse settlements”)	21
IV. Antitrust Law and Cases: The United States.....	23
1. Legal Framework	23
Enforcement.....	24
2. Horizontal Mergers Between Direct Competitors	24
Definitions of Market and Concentration	25
Application to Pharmaceuticals	26
Valeant Pharmaceutical’s acquisition of Sanofi’s Dermik unit.....	27
Johnson & Johnson’s (“J&J”) acquisition of Pfizer’s Consumer Healthcare business	27
Mergers of Retail Pharmacies and Wholesalers	29
3. Potential Competition Mergers	29
Watson’s acquisition of Arrow	29
Pfizer’s acquisition of Pharmacia	30

Barr’s acquisition of Pliva	30
4. Innovation Market Mergers	30
5. Vertical Mergers.....	31
6. Other Monopolization Cases.....	32
Patent “Evergreening”	32
Product Hopping	33
Commentary	34
7. Illegal Tying and Other Arrangements	34
8. Agreements Not to Compete	35
Pay-for- Delay Settlements	35
Agreements on Price or Price-Related Terms	37
9. Price discrimination.....	38
V. Anti Trust and Competition Policy in the EU	39
1. Antitrust Law	39
Market definition	41
Parallel Trade	41
2. Application to the Pharmaceutical Industry	42
Strategies to Delay Generic Entry	42
Strategic Patenting.....	43
Litigation.....	43
Interventions Before National Regulatory Authorities	43
Life Cycle Strategies for Follow-on Products.....	44
Strategic Patenting to Block Competitor R&D	44
Recommendations of the Inquiry	44
Enforcement Action Since The Pharmaceutical Inquiry.....	44
Commentary	45
3. Abuse of Dominance, Misuse of the Regulatory Process and Product Hopping	45
Commentary	46
4. Mergers and Acquisitions.....	46
VI. Conclusions and Implications for Middle and Lower Income Countries (MLICs).....	46
1. Mergers and Acquisitions.....	46
2. Agreements Not to Compete	48
3. Other Monopolization Issues.....	50
References	52

I. Introduction and Overview

The pharmaceutical industry is characterized by atypical economics and an unusual intersection of regulation, patent and antitrust law. The supply side of the industry includes originator and generic prescription and over-the-counter (OTC) drugs, in addition to wholesalers and retail pharmacy services. Each of these sectors has some distinctive features that affect application of competition policy. Originator prescription drugs are highly research-intensive and have significant potential market power due to patent protection, regulatory exclusivities and insurance coverage. The generic sector, which may include pure generics and copy products, is potentially structurally competitive, depending on entry and insurance reimbursement conditions. The distribution sectors, which include wholesalers and retail pharmacies, are also potentially structurally competitive. Each of these supply sectors is heavily influenced by regulation in most countries and, in some countries, by the countervailing power of public and private insurers that act as third party payers and agents for patients, the ultimate customers. The functioning of competition and final prices of medicines reflect the combined effect of regulatory, patent and anti-trust policies and the countervailing power of payers.

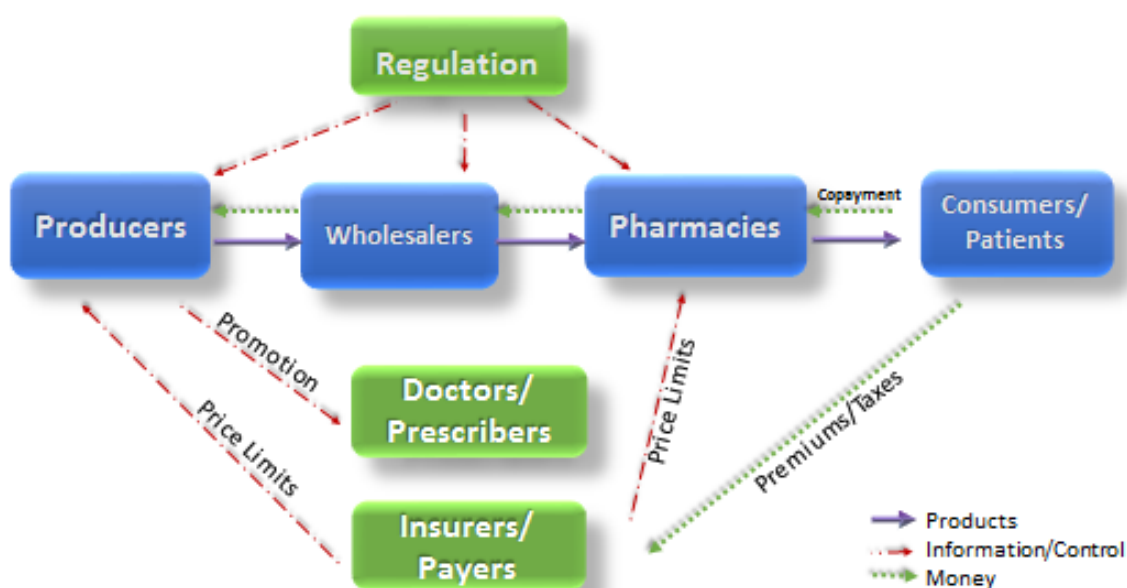
In all countries, pharmaceuticals are subject to extensive market access regulation, because they are technologically complex products that can pose a high but unobservable risk to health. Market access regulation requires that prescription drugs demonstrate safety, efficacy and manufacturing quality as a condition of being generally available to consumers. Access to medicines is further regulated through requirements that they be prescribed and dispensed by licensed physicians and pharmacists, which tends to create market power for these patient agents. Price regulation is pervasive, initially in response to insurance that undermines consumer price sensitivity and creates powerful governmental payers, and also in response to the public health concern that drugs be affordable. Because the details of these regulatory, insurance and agency relationships differ across countries, the role of antitrust and competition policy also differ to some extent across countries, although fundamental principles are similar.

This paper describes antitrust issues related to the pharmaceutical industry, focusing on the production and distribution of prescription drugs, including originator and generic products. OTC products are included to a much lesser extent. Section II describes the major economic characteristics of the pharmaceutical industry that intersect with antitrust policy, including patent and regulatory policies, and the roles of insurers, physicians and retail pharmacies that act as agents for patients/customers. These economic characteristics differ to some extent between originator vs. generic sectors, and between high income vs. middle and lower income countries, as outlined in Section II. Section III provides an overview of the main contexts in which anti-trust actions have arisen in the pharmaceutical industry. Section IV and V describe the case law in the US and the EU, respectively, which have similar market access regulation but differ in the role of private vs. public insurance and in payer use of countervailing power, and other factors. Section VI briefly examines antitrust issues in countries with less mature regulatory systems and with predominantly self-pay markets for outpatient drugs, and draws conclusions.

II. Economic and Policy Background

This section provides background on the two major producer sectors, Originators and Generics, and the Retail Pharmacy sector, focusing on how their economic fundamentals and the role of regulation, patents, physicians and insurance reimbursement affect competition dynamics. The first three subsections describe these sectors in high income countries, where regulation and insurance are most developed, and subsection 4 discusses relevant differences in middle and lower income countries.

The Pharmaceutical Value Chain: Flow of Goods, Information and Money



1. The Originator Pharmaceutical Sector

R&D, patents and exclusivities

Originator drugs are novel compounds that are characterized by high costs of R&D. The research-based pharmaceutical industry spends roughly 17% of revenues on R&D, compared to an average of 4% for other US industries. The average cost of bringing a new molecular entity (NME) to market is estimated at \$1.5b. (Mestre-Ferrandiz et al. 2012). This high cost per approved NME includes the costly inputs and challenging science of drug discovery, formulation and testing; animal studies and human clinical trials required to meet regulatory standards of safety, efficacy and manufacturing quality; costs related to failures; and the opportunity cost of capital over the 6-12 years required from discovery to approval (DiMasi et al. 2007).¹ This fixed R&D cost is largely invariant with respect to volume sold,

¹ Follow-on molecules and new formulations have lower R&D costs that are not included in the estimated cost per NME approved.

sunk at launch, and “globally joint”, that is, the cost cannot be meaningfully allocated to the different countries in which the drug is sold. In contrast to the high, fixed cost of R&D, marginal production cost per dose is typically low, especially for chemical drugs.

Biologics are pharmaceutical products that are created using biologic processes, rather than chemical synthesis. Biologics on average incur similar R&D costs to most chemical drugs,² but higher production costs.

This originator cost structure of high fixed costs and relatively low variable costs implies that patents are essential to enable originator firms to potentially recoup their R&D investments. Patents are a government grant of monopoly status that bars copies of the patented product for the duration of the patent, in order to enable the originator to charge prices above competitive levels. The WTO Trade-Related Aspects of Intellectual Property Rights (TRIPS) provisions require that all WTO member countries recognize 20 year product patents, running from date of filing. Individual countries retain certain flexibilities, including: requirements for patent eligibility (definition of novelty, etc.); compulsory licensing; and rules governing international exhaustion and parallel trade.

Regulatory exclusivities supplement this patent-based monopoly power of originator pharmaceuticals in most high income countries. Unlike patents, these regulatory exclusivities differ across countries and cannot be challenged by competitors. They include: patent term extension (US) or supplementary protection certificate (EU) of up to 5 years after patent expiry, to compensate for time lost obtaining regulatory approval; a data exclusivity period from originator approval, during which generics may not reference the originator’s clinical data to obtain regulatory approval;³ a 6 month patent extension (US) for doing pediatric trials; and varying exclusivity periods for new formulations that require clinical trials. The US also grants a 7 year market exclusivity for orphan drugs.⁴

In some technology-intensive industries, patent terms are relatively unimportant because economic obsolescence makes most patents irrelevant before the 20 year patent term expires. By contrast, pharmaceutical patents tend to convey significant market power until patent expiry and generic entry. Thus the setting of patent terms and regulatory exclusivity periods for new medicines is an important policy question. Unfortunately, the economic theory underlying patents provides no unique patent term that is optimal for all products and industries. The 20-year TRIPS patent term and the various regulatory exclusivities thus reflect political compromises that are probably of varying appropriateness for different drugs and countries.

Despite – or because of – strong patents on originator molecules, innovator firms race to innovate in new and existing disease classes. This leads to dynamic competition between multiple, differentiated, patent-protected originator molecules (“therapeutic substitutes”) in each class within a few years from the launch of the first-in-class drug. Thus even before generic entry, most pharmaceutical markets are better characterized as oligopolies rather than monopolies. Important

² Dimasi et al. 2007.

³ In the US, the data exclusivity period is 5 years for chemical drugs, 12 years for biologics. In the EU it is 10 years for all drugs.

⁴ In the US, the Orphan Drug Act (1983) defines an orphan drug as a drug to treat a disease that affects fewer than 200,000 patients. The FDA designates drugs as eligible for orphan status. Orphan drugs receive a 7 year market exclusivity that is separate from data exclusivity or patent status, in addition to special R&D tax credits. The EU defines orphan diseases as those affecting less than 1 in 2,000 persons or a maximum of 250,000 in the EU (Regulation (EC) No. 141/2000) and provides for 10 years of market exclusivity.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000392.jsp&mid=WC0b01ac058061f019.

exceptions occur for very small disease areas, where sales may be too small to attract multiple originator products. However, because prices tend to be higher for small disease classes, especially for orphan drugs, even some orphan classes have attracted multiple competing products.

Regulation of Market Entry: Safety, Efficacy, Quality and Promotion

Entry to pharmaceutical markets is heavily regulated, in order to protect consumers from the risks of harm to health and/or wasted expenditure on ineffective products. Because pharmaceutical safety and efficacy are intrinsically unobservable, governments in most countries require that pharmaceutical products that pose potential health risks or wish to make health claims must meet strict regulatory requirements as a condition of market access. Agencies such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) require that all new drugs undergo specified laboratory, animal and human testing in controlled clinical trials, to provide evidence of safety and efficacy as a requirement for market access. Pharmaceuticals are also subject to current good manufacturing practices (cGMPs) standards and pharmacovigilance requirements to report adverse events throughout product life. The conduct of clinical trials by originator drugs typically takes 4-6 years, and regulatory review adds an additional 1-2 years, implying a substantial time and cost barrier to entry of originator drugs.

Most high income countries also regulate pharmaceutical promotion. For example, the US FDA requires that companies only make promotional claims that are supported by evidence from clinical trials. Direct-to-consumer advertising of individual branded drugs is banned except in most countries except the US and New Zealand. Other countries permit informative (“help seeking”) advertising to consumers, provided that the information is limited to the availability of treatment for specified symptoms, without naming individual products.

Insurance coverage and price regulation

Most high income countries cover prescription drugs as part of their comprehensive health insurance systems. Insurance coverage provides financial protection to consumers but thereby makes consumer demand inelastic. Price-insensitive demand creates incentives for manufacturers to charge much higher prices than would occur as a result solely of patent-based monopoly power. For example, if the insurance requires a fixed consumer co-payment – say \$25 -- per prescription, consumer demand is totally inelastic at prices above \$25, which creates incentives for manufacturers to raise prices.

To constrain this price-increasing effect of insurance, insurance payers in almost all high income countries regulate originator drug prices either directly or indirectly, as a condition of insurance coverage. To obtain approval of reimbursement coverage and price, an originator company must typically submit evidence of a drug’s effectiveness and economic impact, compared to established, standard-of-care drugs. This evidence is reviewed by a governmental or quasi-governmental agency with expertise in evaluating data on clinical outcomes, effectiveness and economic impact, relative to comparator drugs, to justify price and reimbursement. These insurance-driven limits on drug prices as a condition of reimbursement are best analyzed as a potentially efficient response by insurance payers to the price-increasing effect of insurance, not as an attempt to control monopoly power.

More specifically, these price regulatory systems use two basic approaches to determine a limit on the price of an originator drug:⁵

Internal referencing compares the price of the new drug to prices of similar, existing drugs, and requires evidence of incremental clinical benefit in order to justify a higher price. Cost-effectiveness

⁵ For more detail, see Danzon (2012).

thresholds (as used by, for example, NICE in England) and value-based pricing are special forms of this approach. They effectively calibrate the price premium over existing drugs based on evidence of incremental health gain relative to the comparator drug.

External referencing limits the price of the new drug in the regulating country to the lowest, median or mean price of the same drug in a specified set of reference countries. This approach has the effect of constraining price discrimination between countries, although this may not be the explicit rationale.

These price regulation systems, operated by (or on behalf of) health insurance payers, can control the potential for abuse of market power by originator drugs that arises because insurance exacerbates the demand inelasticity due to patents and regulatory exclusivities. Use of price regulation to control the effects of insurance is potentially efficient, if rules are designed with a view to static and dynamic efficiency.⁶ Such price regulation should not be viewed as simply a control over patent-based market power, because patent are an intentional government grant of monopoly power to incentivize R&D. Rather, the rationale for drug price regulation arises primarily because insurance undermines consumers' price elasticity and hence undermines the ability of market forces to constrain prices to patent-based monopoly levels, as occurs in other industries where patenting is common. In countries where private insurance is supplementary to public insurance, the public payer rules for drug pricing sometimes but not always apply to the supplementary private insurance.

Market pricing in the US In the predominantly private US health care system, payment for outpatient drugs is largely managed by private health plans and pharmacy benefit managers (PBMs). PBMs are specialized intermediaries that are contracted by health plans and self-insured employers to manage pharmacy benefits. No single health plan in the US has sufficient authority or market power to control drug prices.⁷ However, health plans do attempt to constrain their pharmaceutical expenditures by using PBMs to negotiate discounts and steer usage to lower priced drugs. Specifically, PBMs create tiered formularies of reimbursed drugs with associated tiered co-payments, to provide financial incentives for patients/physicians to choose drugs that are on preferred tiers with lower co-payments. The ability of PBMs to shift market share towards preferred drugs enables them to negotiate price discounts from drug manufacturers in return for preferred formulary placement of their drugs. PBMs also directly control access to expensive drugs by requiring prior authorization and/or that patients first try cheaper drugs ("step edits"). Similarly, PBMS negotiate reduced dispensing fees and margins from pharmacies, as a condition for pharmacies to participate in the PBM's network of pharmacies eligible for reimbursement. PBMs have played an important role in encouraging generic substitution, by offering consumers much lower co-payments (\$0-\$10) on generics compared to \$45-\$90 on off-patent originator brands. These techniques of pharmacy benefit management do not set ceilings on drug prices but they do generate discounts on drug costs and pharmacy fees that outweigh the added administrative costs, compared to unmanaged drug coverage. Over time, some large health plans have developed their own in-house PBMs, but many still contract with independent PBMs to manage their pharmacy benefits. From an antitrust perspective, health plans and PBMs play an important role as potentially price sensitive customers/agents for patients, that can exercise some countervailing power to constrain the price-increasing effects of insurance that might otherwise be exploited by drug

⁶ See Danzon et al. (2013b).

⁷ Although the public health insurance programs (Medicare, Medicaid and other smaller programs), collectively pay for almost 50 percent of pharmaceutical expenditures in the US, these public programs are fragmented, are restricted by statute from negotiating drug prices and to a large degree rely on private plans to operate their coverage. For details, see Danzon (2014).

manufacturers and retail pharmacies. However, concentration in the PBM industry is also a potential concern.

Physician Agency

In high income countries, drugs that pose significant health risks require a prescription (Rx) from a physician or other licensed practitioner. By contrast, drugs that are deemed to pose low risks are available without prescription, either “over-the-counter” (OTC) as in the US or “behind the counter” (with advice from the pharmacist) as exists as a third category in many EU countries, such as the UK.⁸ OTC products are generally not reimbursed by insurance. This strict Rx/OTC distinction in high income countries contrasts with many MLICs, where pharmacists in practice often dispense nominally Rx drugs without a doctor’s prescription.

Physician agency for patients in deciding whether/which drugs to prescribe tends to make demand more inelastic, because physicians are unaware of drug prices, and such price-insensitivity is rational if the patient- principals are also price-insensitive due to insurance.⁹ Given the high margin of price over marginal cost for originator drugs, originator manufacturers invest heavily in promotion to physicians. This promotion focuses solely on brand and clinical benefits of the drug, not the price, and the same is true of direct-to-consumer advertising in the US. The fact that promotion is often more important than price in determining market shares, because consumer demand is price-insensitive due to insurance, is important for antitrust approaches to market definition that rely on price elasticity.

Drugs that have proven to be extremely safe are occasionally switched from Rx to OTC status in the US, which leads to lower prices. Unfortunately, because the OTC switch also entails loss of reimbursement, it is not possible to determine how far this OTC price drop reflects elimination of insurance coverage vs. elimination of physician intermediation, which enables consumers to select drugs directly and see prices before purchasing at the pharmacy.

Empirical evidence from different countries and contexts confirms that targeted financial incentives for physicians and/or hospitals, who are decision-making agents for patients, can be effective in constraining drug prices. In particular, when insurers structure reimbursement such that physicians or hospitals are financially at risk for the cost of drugs that they prescribe, drug prices and use are constrained. For example, in the 1990s Germany implemented a “drug budget,” which put outpatient physicians at risk for the cost of drugs they prescribed. This constrained prices and use of drugs (Schoffski et al. 1997). Similarly, in countries where hospitals are paid a fixed reimbursement per patient admission (a “DRG payment”) that includes the cost of drugs, hospitals are incentivized to be cost-conscious in their use of drugs.¹⁰

2. Generics

The US FDA defines a generic drug as “a drug product that is comparable to a brand/reference listed drug product in dosage form, strength, route of administration, quality and performance

⁸ Some European countries further divide OTC drugs into those that can only be sold by licensed pharmacies vs. those that may be sold through supermarkets etc.

⁹ Additional distortions arise when physicians also dispense the drugs that they prescribe, because they can profit from the margin between their acquisition cost and the reimbursement price. Physician dispensing was traditionally common in some Asian countries such as Japan; recent policies have reduced but not eliminated this practice. Physician dispensing of infusion drugs remains common in the US.

¹⁰ See Danzon (2012) and references therein.

characteristics, and intended use”.¹¹ Performance characteristics are measured by bioequivalence.¹² Some countries – particularly middle and lower income countries --have traditionally permitted a broader category of “similar” or branded generic products that claim similarity to the originator but have not demonstrated proof of bioequivalence. Over the last decade, some of these countries have moved to establish regulatory standards for “interchangeable” generics, that is, generics that meet regulatory standards of bioequivalence to the originator reference drug and are therefore eligible for substitution by pharmacies. However, even if deadlines for similars to comply with interchangeability standards exist, these are not always fully enforced. We return to the discussion of similars in section II.4. Counterfeits are a third category of copy products that make fraudulent claims to be branded products that they are not. The existence of counterfeits exacerbates consumers’ uncertainty about generic quality, but these are issues of fraud that are not discussed here.

Generic versions of chemical drugs by definition have an active ingredient that is chemically identical to the originator drug and therefore incur minimal R&D costs. Because chemical generics are potentially low cost, undifferentiated products that have met the same bioequivalence and manufacturing quality requirements as the originator, generic markets are potentially structurally highly competitive, provided that entry regulations and other competition policies are designed to assure low entry costs and competition on price, rather than brand, as described below.

Follow-on biologic drugs are more difficult to characterize as identical to the reference product, because biologics manufacturing uses natural entities and processes. Reflecting these potential differences, “generic” biologics are called “biosimilars”, and are subject to more extensive regulatory requirements for testing and clinical trials than are chemical generics, with requirements varying with complexity of the biologic molecule. Regulatory rules for biosimilars approval have been developed by the EMA and are being developed in the US, and several other countries have followed the EMA lead, with various modifications. The expectation is that most biosimilars will face significantly higher costs of R&D, regulatory approval and production than chemical generics, leading to fewer biosimilar entrants and more oligopolistic markets for biosimilars. No biosimilars have yet been approved in the US, but several are already marketed in the EU and in other countries. Reimbursement and pharmacy substitution rules are still evolving, and will likely be critical to the extent and nature of competition in biosimilars markets.¹³

Market Access Regulation of Generics

Generics can potentially provide huge savings to consumers because of their lower costs and competitive market structure. However, a necessary condition is that consumers, doctors and payers have confidence that generics are of comparable quality to originator drugs. Most high income countries therefore require that generics meet the same standards of safety, efficacy and quality as originator drugs, but permit generics to meet these requirements by demonstrating bioequivalence to the reference originator drug, rather than conducting new safety and efficacy trials.

In the US, the 1984 Drug Price Competition and Patent Term Restoration Act (known as the Hatch-Waxman Act) laid the regulatory framework for generic entry, with a view to reducing costs and

¹¹ US FDA. “Generic Drugs.” Center for Drug Evaluation and Research.

<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm127615.pdf>

¹² A generic drug is considered bioequivalent if it contains the same active pharmaceutical ingredient as the originator drug, is the same dosage, strength and form, and exhibits a similar rate and extent of absorption. FDA Center for Drug Evaluation and Research, Approved Drug Products with Therapeutic Equivalence Evaluations (32d ed.), <http://www.fda.gov/drugs/developmentapprovalprocess/ucm079068.htm>

¹³ See Grabowski, Long and Mortimer (2014).

expediting generic entry.¹⁴ Specifically, Hatch-Waxman established an Abbreviated New Drug Approval (ANDA) process for generic approval. If a generic can demonstrate bioequivalence to the originator, the generic is not required to demonstrate safety and efficacy through new clinical trials but can simply refer to the originator's trials ("data"), once the originator's data exclusivity has expired. Generics must meet the same cGMP and inspection standards as originators. Generics that meet bioequivalence requirements are designated as substitutable by the FDA ("AB-rated") for the referent originator drug of the same active ingredient, formulation, strength and route of administration. In the US, non-substitutable generics exist mainly for products with high therapeutic risk and for formulations such as creams and liquids for which standard bioequivalence testing is not feasible.

Since the 1980s, all states in the US have enacted pharmacy substitution laws for chemical generics. Specifically, pharmacies may substitute any AB-rated generic for the originator brand, unless the physician explicitly requires the brand. Thus pharmacy substitution is the default from which a prescriber must opt out, rather than an option to which prescribers must opt in. Pharmacy substitution implies that pharmacies are the decisive customers for generics, not physicians. Wholesalers are also important customers for generic firms, since wholesalers contract to supply smaller pharmacies.

Patent certification An originator manufacturer that seeks regulatory approval of a new drug must file a New Drug Application (NDA) with the FDA, which includes the patents that are claimed. If the FDA approves the NDA, it lists the drug and the associated patents in its publication known as the Orange Book.¹⁵ The US Hatch-Waxman Act includes a provision that ANDA applicants must certify that either: no patents are listed in the Orange Book (Paragraph I); listed patents have expired (Paragraph II); they are not seeking approval until listed patents have expired (Paragraph III); or that listed patents are invalid, unenforceable or not infringed (Paragraph IV), in which case they must notify the patent holder. The patent holder may then file a patent infringement suit which automatically delays FDA approval of the ANDA for the lesser of 30 months (a "30 month stay") or until the litigation is resolved. The first generic to successfully challenge all the originator's listed patents and file a "substantially complete" ANDA receives 180 days exclusivity as the sole ANDA generic in the market. This first-to-file (FTF) exclusivity was intended to provide an incentive for generics to incur the costs of challenging potentially invalid patents.

Under the 1984 Hatch-Waxman provisions, originators had incentives to file and list follow-on patents ("patent evergreening") in the Orange Book, because generics would have to challenge each listed patent, which added litigation costs and could yield successive 30-month stays, even if the patents had not yet been approved by the US Patent Office. The Medicare Modernization Act (MMA, 2003) limited the number of 30-month stays to one per molecule. State Attorneys General have also filed suits alleging that "frivolous" patenting has delayed generic entry and raised health care costs for payers, resulting in some very large fines. Both the MMA reforms and litigation should deter frivolous patenting.

Because generic entry typically results in a dramatic reduction in market price of the drug, both originator and generic entrant(s) can potentially profit if they can agree to delay generic entry, to prolong and share the monopoly rents. These "pay-for-delay" agreements between originator and generic firms have been a major area of anti-trust litigation in both the US and the EU (see section IV:8). In the US prior to the MMA, the originator had particularly strong incentives to pay the first-to-file (FTF)

¹⁴ For a summary of the regulatory framework for generics, see also the FTC's *Doryx* Amicus Brief http://www.ftc.gov/sites/default/files/documents/amicus_briefs/mylan-pharmaceuticals-inc.etal.v.warner-chilcott-public-limited-company-et-al./121127doryxamicusbrief.pdf, and references therein.

¹⁵ In the US patents are reviewed and granted by the US Patent Office (PTO), which may take 2-4 years, not by the FDA. Patents may be listed in the FDA Orange Book even if their review is still pending.

generic to delay entry, since delay in triggering the 180-day exclusivity would delay the entry of other generics, thereby prolonging the monopoly pricing period. The MMA provided that if the FTF generic is not able to market its product at the time the exclusivity is triggered, it may waive its exclusivity in favor of another specific generic company. But an FTF generic may forfeit its exclusivity if it fails to enter within 75 days of FDA approval. In that case, the exclusivity passes to the next FTF generic in line, if any exist; if none are in line, the exclusivity is forfeited and any other waiting generics may enter.

Reimbursement of generics

In the US, the bioequivalence requirement enables doctors, patients and payers to treat generics as equivalent to originator products. Payers therefore set one maximum reimbursement price that is the same for all substitutable generics and the originator. This is called a maximum allowable cost (MAC) in the US or a reference price (RP) in EU countries that use this approach. The MAC or RP is usually based on the market price of a relatively low-priced generic. Because pharmacies can profit from the difference between the MAC and their acquisition price, generic producers compete by discounting below the MAC, in order to maximize the margin captured by their pharmacy customers. Payers capture some savings from competition by revising down the MAC periodically, based on an audit of actual market prices. This in turn triggers another round of generic price competition. Further, US payers incentivize patients to accept generics through lower co-payments.

A few countries (e.g. Japan) regulate the reimbursement for generics (and/or maximum generic price) to a percent – say 60-70 percent -- of the regulated originator price. Regulating a maximum reimbursement price has been counter-productive, because the maximum becomes a minimum for list prices charged by generic firms to payers. This is exacerbated when the generics receive different reimbursement code(s) from the originator. In this context, even if pharmacies are authorized to substitute, originator firms and/or high priced generics are able to offer bigger discounts to pharmacies than can generics with lower reimbursement prices, which undermine pharmacy incentives to substitute towards cheaper products. In some cases, generic firms compete for market share by discounting to pharmacies below the regulated price, but these discounts accrue as profit to pharmacies, not as savings to payers if they keep the reimbursement for generics set at the 70% of the originator price.

Although the US has relatively high prices for originator drugs, the US approach to generics results in low priced, high quality generics and very significant savings from generic substitution. In this system, the bioequivalence requirement is essential to eliminate concerns about generic quality, such that competition focuses on price. Bioequivalence also eliminates the rationale for branding and promotion by generics, forcing generics to compete on price rather than brand. Most US generics are in fact unbranded and incur minimal marketing effort or expense. In this context, generic promotion of brand to doctors, patients or payers would be wasted expense, because pharmacies can substitute and are motivated mainly by price. Consequently, in the US generic prices fall to 10-30 percent of the originator price and generics capture 80-90% of prescriptions within several months of entry of multiple generics. The optimal originator strategy in response to generic entry is to cease all promotion and possibly raise rather than lower price, retaining only the tiny percentage of originator-loyal customers who are price-insensitive. Many originator firms also license a generic producer to produce and sell an “authorized generic”, sold under a generic name and priced below the originator, in order to capture some of the price-elastic customer segment. Since the 2000s, most major EU markets have adopted

pharmacy substitution and reimbursement incentives to encourage generic adoption and price competition that in some respects resemble the US model.¹⁶

In summary, both theory and empirical evidence from different high-income countries confirm that establishing a pharmaceutical market with widely accepted, high quality, low priced generics requires certain regulatory and competition policies, including: regulatory requirements for bioequivalence and high cGMP standards, to eliminate quality uncertainty; legal authorization for pharmacies to substitute between bioequivalent generics; financial incentives for pharmacies to be price-sensitive in their purchasing and compete on price to consumers; and incentives for consumers to accept generics.

3. Retail Pharmacies

Most countries require that prescription drugs be dispensed by licensed pharmacists who can act as informed agents for relatively uninformed consumers. Pharmacists also play an important role advising patients on use of over-the-counter (OTC) medicines, nutritionals and other health products that do not require a physician prescription. Licensure requirements for pharmacists, as with any professional licensing requirements, restrict competitive entry into the practice of dispensing pharmaceuticals and other restricted products, with the intended benefit of assuring safe drug dispensing and sound information for patients.

The restriction on competition, that prescription drugs must be dispensed by a licensed pharmacist, is exacerbated in some countries by more questionable restrictions on the number, location and ownership of retail pharmacies. These restrictions include: limits on the location of pharmacies; requirements that pharmacies be owned as well as operated by a licensed pharmacist; limits on chain formation and/or the number of stores in a chain; restrictions on online and mail order pharmacy; restrictions on supermarket and other mass market ownership of retail pharmacies; restrictions on what types of store can sell over-the-counter drugs, etc. Such restrictions have traditionally been common in the EU (excluding the UK) but are slowly changing.¹⁷ By contrast, the US permits commercial ownership of pharmacies and pharmacy chains; permits supermarkets and other mass merchandise stores to establish pharmacies, staffed by licensed pharmacists; and permits mail-order dispensing of drugs by licensed pharmacies, including PBM mail pharmacies. The rationale for permitting competitive entry and commercial ownership of retail pharmacy businesses are several: that pharmacy ownership is unimportant, provided that drug dispensing is done by a licensed pharmacist; commercial ownership facilitates raising capital, which is necessary to take advantage of scale economies; and that competitive entry serves as an important constraint on the potential market power of retail pharmacies.

The available evidence from the EU suggests that policies to promote competitive entry to retail pharmacy have been beneficial for consumers.¹⁸ In the US, competitive market pressures have supported a trend towards acquisition of independent, family-owned pharmacies by commercially-owned chains, which benefit from economies of scale and scope in purchasing, operating electronic data interface with payers and suppliers, and offering long hours, convenient location and broad product choice for consumers. Competition between local retail pharmacies in different chains has remained robust in the US, due partly to antitrust action that has blocked pharmacy acquisitions in areas of

¹⁶ Danzon, P. and Furukawa M. "Cross-National Evidence on generic Pharmaceuticals: Pharmacy vs. Physician Driven Markets." National Bureau of Economic Research. July 2011. <http://www.nber.org/papers/w17226.pdf>

¹⁷ For detail, see IMS (2010); Lluch (2010); Volkerink et al. (2007).

¹⁸ See Volkerink et al. (2007) for EU experience. In the US, the growth of pharmacy chains, supermarket and mass merchant pharmacies provides strong "survivor" evidence of efficiency gains from permitting diverse commercial ownership of retail pharmacies.

potential market power, and to ease of entry into pharmacy ownership by mass merchandise stores such as Walmart and supermarkets. The retail pharmacy chains, such as Rite-Aid and Walgreens, have in turn engaged in competitive expansion into selling groceries, small appliances etc., and primary care services including vaccinations and Minute Clinic consultations that offer a convenient and inexpensive alternative to a physician visit.

The potential market power of pharmacies that could result from their monopoly over drug dispensing is counteracted by powerful third party payers in high-income countries with comprehensive insurance, as discussed above (Section II:1). Public insurers that regulate ex-manufacturer drug prices usually also limit the markups added by wholesalers and retail pharmacies, in order to control the final drug prices that retail pharmacies charge to payers/consumers. Similarly in the US, private health plans use their countervailing power to limit the distribution margins and dispensing fees charged by pharmacies. PBMs typically establish networks of “preferred pharmacies” from which insured consumers must obtain their drugs, and preferred pharmacies must accept limits on their reimbursement and dispensing fees as a condition of participating in the network and thus qualifying for the insurer’s business. For example, a PBM may cap payment to the pharmacy for drugs at X percent of the drug’s list price, pay \$1-3 per prescription as a dispensing fee and specify the co-payments that the pharmacy can collect from patients, thereby limiting each component and the total retail price charged by the pharmacy. Ultimately the prices health plans/PBMs pay to pharmacies are market-determined: a PBM/health plan must compensate pharmacies sufficiently to attract enough pharmacies to participate in its network such that the health plan is attractive to consumers. Large PBMs also operate their own mail-order pharmacies which offer mail delivery for medications with lower patient cost-sharing than required by retail pharmacies, thereby putting additional competitive pressure on retail pharmacies.

Thus in countries where public payers regulate drug prices and pharmacy margins, such regulation reduces the need for antitrust enforcement to monitor potential abuse of market power over drug dispensing by retail pharmacies. Similarly in the US, health plans and PBMs act as large, well-informed purchasers that ensure competition among retail pharmacy chains. Recognizing the countervailing role of PBMs in constraining drug prices, US antitrust authorities have scrutinized and constrained the vertical mergers between pharmaceutical manufacturers and PBMs (see Section IV:5).

4. Pharmaceutical Markets in Middle and Low Income Countries (MLICs)

Pharmaceutical markets in MLICs share some of the basic characteristics of high income countries described above. This section describes differentiating features for purposes of competition and antitrust policy.

Originator drugs

R&D is a global joint cost, that is, the basic costs of drug discovery and development cannot be attributed to specific countries, and incremental country-specific R&D cost is usually modest, limited to the cost of obtaining regulatory approval.¹⁹ This raises the question of how companies can and, from a social welfare perspective, optimally should recoup these joint costs of R&D. The theory of price discrimination suggests that a profit maximizing monopolist will price discriminate between separable markets, setting prices inversely related to elasticity of demand.²⁰ Economic theory suggests that the price differentials implied by monopoly price discrimination are consistent with socially optimal price *differentials* suggested by Ramsey pricing to optimally recoup joint costs. Absolute price levels should

¹⁹ A few countries (e.g. China, Japan) require clinical trials on local populations. Some drugs may also require adapting for local disease variants (e.g. antivirals and vaccines for specific strains of a virus).

²⁰ Malueg and Schwartz (1994), Valletti, and Szymanski (2006).

plausibly be related to differences in per capita income, but theory cannot establish the exact relationship.²¹ In practice, the evidence suggests that the empirical price elasticity of drug prices with respect to average per capita income is low, implying that on average prices are higher, relative to average per capita income, in lower income countries (Danzon, Mulcahy et al., 2013a).

The adoption of TRIPs patent regimes, including 20 year product patents, has heightened concerns over pricing of originator drugs in MLICs, raising issues of affordability, both for public payers and for consumers who pay out-of-pocket for most outpatient drugs in MLICs. Public payers/governments in MLICs generally limit or regulate prices of the drugs they pay for, as a condition of the drug being on the reimbursement list, sometimes using direct price regulation similar to high income countries or competitive tendering, if close substitutes exist. Some form of price/reimbursement limit is consistent with the rationale of payers counteracting the price-increasing effect of insurance. The optimal design of price/reimbursement limits is discussed in Danzon, Towse et al. (2013b). Price regulation may reduce the need for antitrust scrutiny of pricing. Tendering is intended to stimulate competition, but need antitrust scrutiny to make sure the bidding process is truly competitive.

Some governments also regulate prices for some non-reimbursed, self-pay drugs, with the political rationale of assuring affordability for patients. Because self-pay markets avoid the price-increasing effects of insurance which undermines consumers' price-sensitivity, price regulation is harder to rationalize for on-patent drugs that are paid for directly by patients. Patents may result in originator pricing power but this is the theoretical purpose of patent regimes, although there remains the issue of optimal design of patent regime, in terms of balancing incentives for innovation vs. welfare loss due to pricing above marginal cost. For generics, price regulation should be unnecessary if generic markets are structured to encourage competition on price, rather than brand.

In fact, the optimal design of competition and regulatory policy to control drug prices in self-pay contexts raises important issues for future research, including the following. First, originator prices may be perceived to be excessive because the TRIPs 20-year patent regime may not be optimally designed for these countries for several, not mutually exclusive reasons: (a) since patents were not adopted voluntarily but were required as a condition of WTO membership, there is a presumption that these countries perceive that the welfare loss to current consumers from patents exceeds their expected welfare gain from stimulus to innovation. This is certainly plausible for follow-on formulations of existing molecules (see below); (b) some MLIC countries may experience a net welfare loss from 20 year patents because their demand has negligible impact on innovation which is incentivized by global demand that is dominated by larger, higher-priced countries. This creates an incentive for each MLIC country to free ride, even though in aggregate the MLIC share of global pharmaceutical sales is projected to equal that of the US by 2016 (IMS, 2012); (c) although patent regimes are intended to encourage domestic innovation in MLICs, pharmaceutical R&D is so costly and geared to cutting edge science that few MLIC producers may be able to benefit from patents, to offset the loss to domestic generic manufacturers from patent restrictions on developing copy products. In addition to non-optimal patent regimes, theory and evidence suggest that skewed income distributions in many MLICs can lead originators to adopt prices targeted to the wealthiest minority, which makes the drugs unaffordable for lower income subgroups (Flynn et al. 2009; Danzon et al. 2013a). Further, firms may perceive that if they charge a low price in lower income countries, higher income countries will "import" these low prices through external referencing and/or parallel trade. Although the answers to these questions are beyond the scope of this report, they are mentioned as part of the context to be considered in evaluating competition policy towards originator prices in MLICs.

²¹ Ramsey (1927), Danzon (1997), Danzon, Towse et al. (2013b).

In practice, countries use a range of strategies. Several countries limit the scope of patentability, with the effect if not the intent of constraining prices. In particular, Article 70(3) of TRIPS exempts from patents drugs that were in the public domain before January 1 1995 (Chaudhuri, 2011), but permits patents of new formulations, combinations and chemical derivatives (salts, esters) of these older NMEs. Countries have discretion whether they consider such follow-on products to be novel and therefore patentable. For example, Section 3(d) of India's amended Patents Act denies patents for new formulations "unless they differ significantly in properties with regard to efficacy." This is a high bar, if incremental efficacy is unknowable before a drug is in widespread use, at which time multiple copies may be on the market. India has used Section 3(d) to deny patentability of several products that are widely patented in other countries, for example, Novartis' Glivec. Some countries have also used compulsory licensing to address individual drug prices that are deemed to be excessive. Compulsory licensing is permitted in principle under TRIPS, although there is no consensus on when this is appropriate.²² Compulsory licensing is likely to be most effective at reducing prices if more than one generic company is licensed to produce the drug. The mere threat of compulsory licensing is usually but not always sufficient to bring down the originator's price.

Going forward, it is likely that insurance coverage of outpatient drugs will expand in MLICs, through expanded public and private coverage. This will increase the potential for third party payers to use information and countervailing power to constrain the prices charged by drug manufacturers and margins added by pharmacies. This is not to say that expanding insurance in practice necessarily raises general consumer welfare. In practice, both public and private insurers can introduce market distortions, including undermining consumer price sensitivity which leads producers to raise prices; further, insurers may themselves operate inefficiently and/or be subject to provider "capture". The point here is simply that the existence of countervailing power of powerful payers changes the context and may – if well-designed – reduce the need for antitrust vigilance over providers in MLIC markets.

Generics

Similar and other copy products are common in most MLICs, whereas regulatory requirements that generics demonstrate bioequivalence are relatively recent and not uniformly adopted or enforced. Because the equivalence and quality of these similars is not assured by regulation, they compete as branded generics, using brand and price as proxies for quality. Branded generics invest heavily in promoting their brand to physicians, consumers and pharmacies, which adds real input costs. Empirical evidence confirms that in branded generic markets, average "generic" prices remain at 50-90% of originator prices, despite multiple competing products, resulting in prices that are higher, relative to originators and higher absolutely than generic prices in some high income countries, such as the US.²³ Originator brands also retain significant market share after patent expiry in many MLICs with branded generics. The originator brand retains value as the best guarantor of quality that some consumers are willing to pay for if generic quality is uncertain. Interchangeable generics remain a relatively small segment and price competition among generics and off-patent originator drugs remains weak in most MLICs. Such generic markets forego much of the large potential for savings from generics.

²² India's recent use of compulsory licensing of Nexavar was novel in including the rationale that the very high price was tantamount to not exercising the patent, despite a patient assistance program for low income patients. However, even the generics that were licensed to enter were priced out of reach of the majority of Indians. More generally, to require that companies make their drugs affordable, regardless of the income of the population, is not a sustainable policy in the long run.

²³ Danzon and Furukawa (2011), Danzon, Mulcahy and Towse (2013a).

Many MLICs have enacted bioequivalence regulations and set target dates by which all generics should meet these requirements. Some countries have also adopted other policies to encourage the shift from a generics market that is focused on branding to one focused on price. Experience from countries in the EU and Japan, that have either recently made the switch or are in the process of doing so, shows that these policies include: encouraging physicians to prescribe by international, non-proprietary name (INN) rather than brand; designing prescription pads so that the default is that pharmacy substitution is permitted, unless the physician explicitly requires the brand (opt-out rather than opt-in), on a drug-by-drug basis; requirements that pharmacies stock bioequivalent generics; paying pharmacies a fixed dispensing fee, rather than a percent of the price of the dispensed drugs; and modest incentive fees for physicians/pharmacies that prescribe/dispense a target percentage of interchangeable generics. There is no good evidence on which of these policies is most effective, partly because countries typically adopt several changes simultaneously and because their effects depend on other factors.²⁴ Since pharmacies and patients play a key role in dispensing choices, once interchangeability and substitution are permitted, pharmacists' and patients' financial incentives are likely to be critical. This may be easiest where insurance covers drugs, such that pharmacy reimbursement and patients' co-payments can be used to encourage uptake of interchangeable generics. Advertising campaigns to promote awareness of the bioequivalence of interchangeable drugs is also likely to be useful in encouraging market acceptance. Many of these policies to encourage the switch from similar to bioequivalent generics are within the scope of regulatory policy. However, competition policy can play a critical role in monitoring and enforcement.

Some MLICs include some generics within the scope of their price regulations (e.g. India). The evidence from other countries suggests that such price regulation of generics should be unnecessary if all generics were required to meet bioequivalence standards, thereby eliminating quality uncertainty and the rationale for competing on brand rather than price. Moreover, efficient price regulation requires an economically sound basis for setting the regulated prices. India's recently adopted price regulation scheme proposes a form of internal reference pricing that would regulate the prices of generics/similar drugs to the average prices of drugs with at least 1% of the relevant market. If low price is in fact correlated with low quality, this approach may undermine the incentives of producers to invest in product quality. Further, it may be ineffective at stimulating competition if, over time, all prices tend to converge to the regulated price, with reduced incentive to compete by pricing below the regulated price. Thus although this approach may appear to resemble the MAC reimbursement used in the US or similar RP approaches in some EU countries, in practice it is unlikely to achieve the same results as long as quality is not assured through bioequivalence requirements.

Retail Pharmacies

The market power of pharmacies is often greater in self-pay markets where pharmacies are paid in cash by individual consumers, without the countervailing power of third party payers. Pharmacies in practice often dispense drugs without prescription, and/or may substitute a similar drug even if the patient has a physician's prescription. If pharmacies in practice have discretion in guiding patients' selection of drugs, the regulatory designation of interchangeability only for bioequivalent generics becomes less relevant, unless accompanied by physician and consumer education initiatives.

²⁴ The experience of several EU countries is summarized in Danzon and Furukawa (2011), which also lists country-specific studies for several, including Spain, Italy, Germany, France and Japan.

When consumers pay cash out-of-pocket without a powerful payer to negotiate retail drug prices, pharmacies may have market power in setting retail prices. Further, enforcement of any price regulations that may exist is less easy than in countries where payers enforce the regulated price through direct electronic reimbursement. Market power of pharmacies can also stifle the potential benefits of price competition between originators and generics. For example, even if a generic firm were to offer a low price to the pharmacy, this might simply increase the margin captured by the pharmacy, without benefit to consumers, if retail competition is insufficient to force pharmacies to pass through such cost savings to consumers. Pharmacies that have market power may also maximize their net revenue by not offering generics to patients or by offering only their store-brand generics at above competitive prices, thereby preserving monopoly rents on originator drugs that can be shared between the originator and the pharmacy.²⁵ Chile's requirement that all pharmacies have a minimum stock of all bioequivalent generics should help to counter such anticompetitive strategies by pharmacies.

Consolidation of retail pharmacies into chains can increase this market power of retail pharmacies and facilitate collusive price-fixing on drugs, in local and national markets, as has occurred in Chile. However, chain pharmacies can also offer significant efficiency gains from scale and scope economies in operations. A preferred competition policy may be to permit national chain formation while preserving competition in local markets through antitrust monitoring of mergers and acquisitions (M&A) and facilitating competitive entry of pharmacies in supermarkets and other locations. Legislation to permit supermarkets to sell over-the-counter drugs has been proposed in Chile, but opposed by stakeholders. The experience of the US and several EU countries suggests that supermarkets and other mass merchandise stores can safely operate pharmacies that sell prescription drugs as well as over-the-counter drugs, provided that they meet the same safety requirements as do stand-alone pharmacies with respect to employing a licensed pharmacist to dispense prescription and behind-the-counter drugs.²⁶ Potential entry from such credible competitors can be a valuable check to any anticompetitive threats from chain consolidation of retail pharmacies.

In many MLICs, a significant percent of pharmaceuticals are dispensed through hospitals, including not only drugs for inpatient use but also hospital-owned outpatient pharmacies that compete to some extent with retail pharmacies. Hospital procurement and dispensing of pharmaceuticals can promote competition among drug suppliers, because these large institutional buyers often run procurement tenders that can be designed to select only qualified suppliers and require competition on price. Drug procurement through competitive tendering can achieve significant savings, relative to retail pharmacy prices, in therapeutic categories with multiple competitors (Danzon, Mulcahy and Towse, 2013). There may be a risk that such tenders lead to collusion and division of markets among potential competitors, and competition authorities may play an important role in this. However, it is important to distinguish between market sharing agreements among competing suppliers, which are almost certainly anti-competitive, and market allocation by the customer/purchaser, who may rationally choose to share the market among competing suppliers in order to retain multiple potential suppliers, rather than use a winner-take-all strategy which may lead to withdrawal of other suppliers from the market.²⁷

This brief review suggests some of the ways in which MLIC pharmaceutical markets may pose different issues for antitrust than those encountered in HICs. In particular, promoting robust generic

²⁵ Such cases are analogous in some ways to pay-for-delay cases in the US and EU, except that where pharmacies have market power they may use it to block generic competition and capture monopoly rents themselves.

²⁶ For EU see Volkerink et al. (2007).

²⁷ The US CDC and UNICEF have switched from winner-take-all to rules that facilitate market sharing among competing suppliers for their purchase of vaccines.

competition after patent expiry on originator drugs is an important issue for competition policy in MLICs, as it is in high income countries, although the obstacles to competition differ across countries. Regulatory requirements for bioequivalence of generics are necessary to establish public confidence in quality of generics in MLICs. There may continue to be an important role for active anti-trust enforcement against anticompetitive practices by generic manufacturers and/or retail pharmacies that can benefit from exploiting the quality uncertainty and market power that prevails in branded generic markets in MLICs.

III. Types of Antitrust Cases in the Pharmaceutical Industry

The anti-trust issues that have emerged in the pharmaceutical industry reflect the intersection of the industry's underlying economic characteristics with the patent, regulatory and insurance institutions outlined above.

1. Monopoly and monopolization

In the US, pricing has not been challenged as monopoly issue, despite the continued upward drift of prices, with some orphan drugs now priced at over \$400,000 per patient year. As discussed in Section II.1, high prices reflect patents to incentivize R&D and insurance coverage, hence are better dealt with by payers using insurance control over reimbursement, rather than by antitrust. In the EU and most other high income countries, public payers regulate drug prices as a condition of insurance coverage for drugs and this has pre-empted potential concern over abuse of monopoly pricing power.

Mergers and Acquisitions (M&A), and Licensing Deals

M&A is very common in the pharmaceutical industry, including large horizontal mergers, acquisitions of smaller firms by larger firms, and cross-national mergers. Such mergers are carefully reviewed by US and EU anti-trust authorities for threat of excessive market power at the therapeutic class level. Anti-trust authorities have quite frequently required divestiture of products or product classes of one party to a transaction, where the merger would increase concentration in the relevant markets to unacceptable levels. Several standard anti-trust approaches are used to define markets and market competitiveness, including but not limited to cross-price elasticity concepts. The effects of insurance and physician agency on price sensitivity and hence cross-price elasticities and their use in defining market competitiveness have so far not been explicitly addressed.

Product licensing agreements are very common in the pharmaceutical industry. Most common are deals whereby small firms outlicense their products in development to larger, more experienced firms, in return for financing and expertise in product development and commercialization. Such agreements are typically motivated by financing needs, risk diversification and/or shared expertise, but they may also increase market power, if the outlicensing and inlicensing firms are the sole developers of products for a particular indication. The US FTC recently required that such license deals must be reported for clearance if they are valued above a certain threshold, similar to merger pre-notification requirements.

Patent evergreening and product switching

Monopolies that result from patents are generally regarded as necessary to encourage innovation. However, attempts by originator companies to extend the effective patent life of their drugs by filing patents for additional features or purified forms may overstep the intent of patents and constitute monopolization, in violation of Section 2 of the Sherman Act in the US. Generic companies have sometimes succeeded in asserting private antitrust actions against such practices that harm their ability to compete.²⁸ Extension of effective patent life through the development of new formulations or products that offer negligible therapeutic benefit (so-called product hopping or product switching), simply as a way to block generic entry for the earlier formulation, has been challenged in the US and EU, and may become an area of increased antitrust activity.

²⁸ Bristol-Myers Squibb Co. v. Ben Venue Labs., 90 F. Supp. 2d 540, 543 (2000).

2. Agreements on price

Although most therapeutic classes start out as oligopolies with high entry barriers for new entrants, charges of collusive pricing between on-patent prescription drug manufacturers are rare in the US and EU. In most EU countries, price regulation preempts the potential for collusion to raise price because firms cannot charge more than the regulated prices and have no incentive to charge less.

Although the US permits free pricing, allegations by anti-trust authorities of collusive pricing by originator firms are hard to find. Contributing factors may include product differentiation and, as outlined above, that insurance makes firm-specific demand so inelastic that collusion is unnecessary to maintain high prices. Consistent with the major role of insurance, the one instance of a large and long standing price collusion was for vitamins, which are OTC and not covered by insurance. Such self-pay demand would be much more elastic in the absence of collusion, hence the gain from collusion would be greater. Moreover, the customers for prescription drugs are primarily large payers that are well-informed and active in negotiating discounted prices, in return for preferred formulary positioning. Payer countervailing power against originator prices is most effective in classes with several, clinically similar therapeutic substitutes, such as statins. Payers have less leverage to negotiate discounts in classes with differentiated drugs that are less close therapeutic substitutes. In particular, “specialty” drugs for diseases such as rheumatoid arthritis or cancer, are often biologics that are more clinically differentiated than the older, chemical drugs used by general practitioners to treat mass disease classes. Although payers lack the ability to control specialty drug prices in the US, collusive pricing has not been an issue.

Pharmacy customers have alleged collusive, monopolistic and discriminatory pricing by originator drug manufacturers, in multi-allegation suits that focus on price discrimination. These cases were largely settled privately, and have not been joined by the antitrust authorities, whose focus is harm to competition, rather than harm to individual competitors.

Collusive pricing by generics has also rarely been an issue in the US, probably due to number of potential competitors and low entry barriers. However, at any point in time there may be few suppliers of the active pharmaceutical ingredient (API) for a particular drug, and barriers to entry into API production are considerable in the short term. Thus there has been at least one case alleging anti-competitive agreement and conspiracy to monopolize between a generic company and API producers, leading to restricted supply and large price increases for the finished products.²⁹ This resulted in FTC action and a very large payment.³⁰

Collusive pricing by retail pharmacies has also not been a frequent issue in the US or the EU, plausibly due to the countervailing power of payers as major customers of pharmacies. Regulation of pharmacy margins in the EU and negotiation of pharmacy margins by large payers in the US counteract the potential for collusive pricing by pharmacies.

Price Discrimination

Antitrust law in the US takes the position that price discrimination is illegal only if it is harmful to competition, not just to the individual competitors. Allegations of price discrimination in the US

²⁹ FTC v. Mylan Laboratories, In., Cambrex Corporation, Profarmaco SRI and Gyma Laboratories of America, Inc.2000. <http://www.ftc.gov/enforcement/cases-proceedings/9810146/mylan-laboratories-inc-cambrex-corporation-profarmaco-sri-gyma>

³⁰ The FTC is not authorized to fine companies for violation of anti-trust laws. Rather, the FTC seeks disgorgement of ill-gotten gains, which in this case were returned to injured consumers.

pharmaceutical market have usually been brought by pharmacies as customers of pharmaceutical firms, not by antitrust authorities. In fact, price discrimination in pharmaceuticals is usually beneficial to customers in aggregate, because it increases utilization by offering lower prices to price sensitive customers.³¹ Pharmaceutical customers differ in their willingness and ability to pay for drugs, and this is reflected in their choice of insurance coverage in the US. This creates incentives for pharmaceutical firms to price discriminate among insurance plans using confidential discounting. Because this differential discounting tends to benefit competition overall, the US antitrust authorities have not opposed it, and private suits have generally settled for modest amounts.

3. Agreements not to compete: Pay-for-delay (“reverse settlements”); Authorized Generics

The most common horizontal restraint cases in the US and EU are so-called pay-for-delay cases that involve alleged payments by an originator manufacturer of an on-patent drug to one or more generic companies to delay their entry. The incentive for such payments is large in countries with strong patents followed by aggressive generic entry, such as the US, where generic prices can drop to 80% to 90% of the originator level.³² In such circumstances, both the originator and generics can gain if they can agree to delay generic entry, prolonging and sharing the monopoly rents.

Simple theory suggests that the originator’s incentive to pay potential entrants to delay entry would diminish and, at the limit disappear if the number of potential generic entrants is elastic, such that the originator would have to buy off a large number of potential competitors. The incentives for such payments are therefore greatest where there are significant barriers to entry of multiple generics. In the US, these cases arise most frequently in Paragraph IV contexts, where one or more generic(s) are challenging the originator’s patents, rather than waiting for the patents to expire.³³ The Hatch-Waxman terms may exacerbate incentives for such settlements between the originator and the FTF generic challenger(s), by providing a 180-day exclusivity for the generic to successfully challenge the originator’s patents (see Section II.2 above). In practice in the US, originator brands sometimes do pay off multiple FTF generics to delay their entry, plausibly because competition between multiple entrants reduces their expected profits, such that each would be willing to settle for less. Subsequent potential generic challengers would still face the costs of patent litigation but not get any exclusivity reward, and would face the 30 month stay.³⁴ Further, reverse settlements sometimes include provisions that reduce subsequent generics’ incentives to continue their patent challenges, such as allowing the settling generics to enter if another generic wins a patent challenge or enters. However, pay-for-delay cases are also numerous in the EU, which does not grant any exclusivity reward to the first generic to successfully challenge patents. This suggests that incentives for pay-for-delay settlements exist even without the US’ FTF exclusivity period, plausibly because of the cost and time required for follower generics to develop the technological and manufacturing capabilities, meet regulatory requirements for market access, etc.

The legality of pay-for-delay settlements between originator and generic firms has been extensively litigated in the US. A recent Supreme Court ruling³⁵ rejected the position of the lower court,

³¹ Danzon (1997) and references therein.

³² FTC (2010) Pay-for-Delay: How Drug Company Pay-Offs Cost Consumers Billions

³³ http://www.supremecourt.gov/opinions/12pdf/12-416_m5n0.pdf

³⁴ Ibid. See also <http://www.ftc.gov/news-events/press-releases/2008/02/ftc-sues-cephalon-inc-unlawfully-blocking-sale-lower-cost-generic>. This case was brought on monopolization grounds, under Sherman Act Section 2, whereas previous pay-for-delay cases were challenged under Sherman Act Section 1, as agreements among competitors that unreasonably restrain trade.

³⁵ FTC v. Actavis, Inc. No. 12-416, 570 U.S. __ (June 17, 2013)

which held that such settlements, including payments, are legal provided that they are within the term of the original patent. This scope-of-the-patent approach might be appropriate if the underlying patent were known to be valid, but this is precisely what is at issue. Rather, the US Supreme Court held that courts should review the specific facts surrounding such reverse settlements under a *rule of reason* standard. In so doing, the Court rejected the FTC's position of presumptive illegality, that such payments should be subject to a "quick look" approach, which would presume competitive harm from a settlement involving payment by the originator to the generics, and shift to the defendant the burden of showing that the agreement was justified.³⁶

To consider the welfare analysis of originator-generic settlements, assume initially that patent regimes are efficient, that is, that patents are granted only where the patent-induced welfare gain from stimulus to innovation exceeds the welfare loss from pricing above marginal cost. Under this assumption of the optimality of patents, early generic entry would be inefficient. Optimal policy would permit originator payments to delay entry until the patents have expired, but not beyond, which could be determined only by examining the facts of the case. By contrast, the position that pay-for-delay payments should be *per se* illegal might be optimal if all patents that are challenged or infringed by generics are in fact invalid or non-optimal. If so, any delay in generic entry would reduce consumer welfare. In reality, the more likely situation at least in the US is that there is considerable uncertainty as to whether challenged patents are valid and will withstand challenge. Such uncertainty may exist either because the Patent Office (PTO) may err on initial rulings on patent validity or because such rulings have not yet occurred. The latter circumstance can occur in the US because originator firms can list patents in the FDA Orange Book while patents are still under review by the PTO, which can take years. The FDA lacks the authority or expertise to evaluate patents and therefore treats all listed patents as a bar to generic entry, even if the PTO has not yet ruled on their validity. Although recent legislative changes have limited the incentive for originator firms to file "frivolous" patents in order to delay generic entry, uncertainty remains over whether the PTO will uphold the claims made in all patents that originators may file. In addition to uncertainty about patent validity, a factual analysis is also required to determine whether any payment from originator to generics is a reasonable payment for litigation costs and/or services performed, or whether it is likely a payment for entry delay, in violation of antitrust law. Given these uncertainties, a rule of reason approach to evaluating pay-for-delay settlements seems appropriate.³⁷

Another issue related to generic entry is the launch by originators of "authorized" generics, either produced directly by the originator or by a generic firm under license from the originator, usually in return for a percent-of-sales royalty payment. In the US, originators often launch such an authorized generic during the Paragraph IV 180 day exclusivity period, as a competitor to the challenging ANDA generic.³⁸ Such authorized generics enable the originator firm to capture more of the rents available during the exclusivity period. The authorized generic may be discontinued once other generics enter and the generic price falls. In the US, the FTC has concluded that such authorized generics are not anticompetitive, because they increase competition and reduce prices during the exclusivity period and thereby benefit consumers. This outweighs any modest disincentive effect of the reduction in exclusivity rents on incentives for generics to challenge patents.

³⁶ http://www.supremecourt.gov/opinions/12pdf/12-416_m5n0.pdf

³⁷ See also Thomas F. Cotter, *FTC v. Actavis, Inc.: When is the Rule of Reason Not the Rule of Reason?*, Research Paper No. 13-20, University of Minnesota Law School, 2013.

³⁸ As an originator-produced or licensed product, an authorized generic is approved under the originator's NDA approval and therefore is not deemed to violate the Hatch Waxman grant of exclusivity to the first ANDA generic.

However, in branded generic markets ex-US the launch by originators of authorized generics may be more harmful to competition, particularly if the authorized generic is launched prior to patent expiry and thereby captures significant first mover advantage among generics, which may reduce entry incentives for other, competitive generics. Since early entry by authorized generics can also benefit consumers, through earlier availability of lower priced products, it is an empirical question whether the net effect of such authorized generic is positive or negative for consumers. Answering this question poses empirical challenges due to endogeneity, that is, an originator's decision to license an early authorized generic is not random but is more likely in markets where it is likely to be profitable. Early papers studying this issue did not control for this endogeneity. Appelt's (2010) study of generic entry in Germany does attempt to adjust for the endogeneity of entry. She concludes that "Originators appear to authorize generic entry prior to loss of exclusivity to extract generic profits rather than to deter generic entry." Thus in this context authorized generics were found to primarily redistribute rents between producers, without necessarily harming consumers. However, because the net effect on competition may more negative in more heavily branded generic markets with weaker price competition than Germany, monitoring of such licensed generics arrangements for anticompetitive net effects is appropriate for competition authorities.

IV. Antitrust Law and Cases: The United States

1. Legal Framework and Enforcement

The 1890 Sherman Act outlaws "every contract, combination, or conspiracy in restraint of trade" and any "monopolization, attempted monopolization, or conspiracy or combination to monopolize." Monopolization is conduct by a firm that "unreasonably restrains competition by creating or maintaining monopoly power."³⁹ Most restraints are judged by a "rule of reason" but certain collusive acts, including price fixing, are considered *per se* violations.

The 1914 Federal Trade Commission (FTC) Act bans "unfair methods of competition" and "unfair or deceptive practices." The 1914 Clayton Act prohibits mergers and acquisitions where the effect "may be substantially to lessen competition, or to tend to create a monopoly." As amended by the Robinson-Patman Act of 1936, the Clayton Act also bans certain discriminatory prices, services, and allowances in dealings between merchants. Under the 1976 Hart-Scott-Rodino (HSR) Antitrust Improvements Act, companies that are planning large mergers or acquisitions are required to notify the antitrust agencies prior to a deal valued over \$70m., to allow the agencies to determine whether such deals may violate antitrust law. The HSR threshold value is adjusted periodically. Notification has also been required for exclusive licenses to patents that transfer the right to make, use or sell a product, *unless* the licensor retained the right to manufacture or use the product, in which case the license was considered non-exclusive and no HSR filing was required. Most states have state antitrust statutes that parallel these federal statutes.

A new federal rule recently published will require notification of licenses that transfer "all commercially significant rights" to "any therapeutic area (or specific indication within a therapeutic

³⁹ "FTC Guide to the Antitrust Laws: Single Firm Conduct: Monopolization Defined." Federal Trade Commission. http://www.ftc.gov/bc/antitrust/monopolization_defined.shtm

area)” *even if the licensor retains manufacturing or other rights*. These rules so far apply only to the pharmaceutical industry, including biologics and *in vitro* diagnostics.⁴⁰

Enforcement

The Federal Trade Commission (FTC) and the Antitrust Division of the Department of Justice (DOJ) are charged with protecting the public from anti-competitive behavior. The FTC has become the primary antitrust regulatory authority with respect to the pharmaceutical industry, playing a more active role than the DOJ in industries where consumer spending is high.⁴¹ The Health Care division within the FTC’s Bureau of Competition was formed to investigate and prosecute exclusively healthcare and pharmaceutical non-merger antitrust matters; merger antitrust matters within this industry are dealt with by the Bureau’s Mergers division.⁴² The DOJ handles criminal enforcement against cartel activities such as price fixing, market and customer allocation and conspiracies in domestic and international markets. Many of the FTC’s adjudicative matters are conducted before an FTC Administrative Law judge. Challenges to the FTC’s determinations are typically resolved with consent decrees or by the companies’ abandoning the challenged transaction; to a much lesser extent, the FTC’s determinations are appealed to federal courts of appeals.⁴³

State Attorneys General bring enforcement actions for the antitrust laws of their states. They have been active in seeking damages where noncompetitive behavior results in unnecessarily high prices for the state-run health programs in their states. Private parties may also bring antitrust actions.

2. Horizontal Mergers Between Direct Competitors

Mergers and acquisitions are an important class of transactions scrutinized by the FTC as potentially tending to lessen competition, enhance market power or create a monopoly.⁴⁴ The goal is to identify and challenge competitively harmful mergers before they occur, while avoiding unnecessary interference with mergers that are competitively beneficial or neutral. Common enforcement actions in merger cases include required divestiture of some assets, returning co-marketing or joint venture rights to a partner, or not continuing with the suspect transaction at all.

The FTC applies a range of analytic tools to the available evidence to evaluate the competitive concerns raised by mergers. A merger can enhance market power simply by eliminating competition between the merging parties, such that the merged entity has a unilateral incentive to raise prices or otherwise harm consumers (“unilateral effects”) or by increasing the risk of coordinated or interdependent behavior among rivals (“coordinated effects”).⁴⁵ Enhanced market power of sellers can

⁴⁰ Cernak, Steve et al. “Expanded HSR Rules Require Reporting of Pharmaceutical Patent Exclusive Licenses, All Exclusive Deals Called “Potentially Reportable” By FTC.” November 14, 2013. <http://www.natlawreview.com/article/expanded-hsr-rules-require-reporting-pharmaceutical-patent-exclusive-licenses-all-ex!>

⁴¹ “FTC Guide to the Antitrust Laws: The Enforcers.” Federal Trade Commission. <http://www.ftc.gov/bc/antitrust/enforcers.shtm>

⁴² “Overview of Antitrust Actions in Pharmaceutical Services and Products.” Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>.

⁴³ “FTC Loses Lundbeck Appeal, Opening Door to More Aggressive Pharmaceutical Merger & Acquisition Activity.” Cooley LLP. August 30, 2011. <http://www.cooley.com/showalert.aspx?Show=65445>

⁴⁴ “Overview of Antitrust Actions in Pharmaceutical Services and Products.” Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁴⁵ “Horizontal Merger Guidelines.” U.S. Department of Justice & Federal Trade Commission. August 19, 2010. <http://www.justice.gov/atr/public/guidelines/hmg-2010.pdf>

adversely affect consumers through price increases or through non-price effects, such as reduced quality or variety of products, reduced innovation or services. Evaluating the effects of mergers is usually predictive. The evidence considered often includes levels and expected changes in market shares and concentration in the relevant market(s), including the HHI of market concentration; whether the merging firms have been or likely would become head-to-head competitors (most relevant for differentiated products); evidence of planned changes in prices, output, capacity, product choice etc.; and evidence from customers and other market participants. Market definition is important to specifying the products and geographies affected, the market participants, shares and concentration. The measurement of market shares and concentration is not an end in itself, but is useful to the extent it illuminates the merger's likely competitive effects. Although market definition is not always the starting point, evaluation of alternatives available to customers is always part of the analysis.

Definitions of Market and Concentration

The FTC's "Horizontal Merger Guidelines" provide guidance on the FTC's enforcement practices with respect to horizontal mergers, including market definition.⁴⁶ Market definition focuses on demand substitution, that is, on customers' willingness and ability to substitute between products in response to changes in price or non-price factors (cross-elasticities of demand). Supply responses by other firms are reflected in measures of market participants, market shares etc.

The FTC utilizes the "Hypothetical Monopolist Test" as one tool to determine product markets. A product market contains those substitute products such that "a hypothetical profit-maximizing firm, not subject to price regulation, that was the only present and future seller of those products ("hypothetical monopolist") likely would impose at least a small but significant and non-transitory increase in price ("SSNIP") on at least one product in the market, including at least one product sold by one of the merging firms." To assess unilateral effects of proposed mergers in markets with differentiated products, where market definition and concentration are particularly problematic, an alternative possible measure is net "upward pricing pressure" (UPP).⁴⁷ The calculation of a "gross upward pricing pressure index" (GUPPI) relies on a "diversion ratio," which measures the fraction of unit sales of a product of one merging firm that switch to a product from the other merging firm when the price of the first product increases. Higher diversion ratios indicate a higher likelihood of unilateral price effects. The net UPP compares the gross upward pricing pressure from reduced direct competition with the offsetting effects of marginal cost savings from the merger.

The FTC typically calculates market shares and market concentration using the smallest relevant product market satisfying the hypothetical monopolist test, because the relative competitive significance of distant substitutes tends to be overstated by their share of sales. Thus the product market does not need to contain the full range of products from which customers may choose or substitute in response to a price increase. The FTC uses a flexible benchmark of 5% of the pre-merger benchmark price for the purposes of determining whether the merger would result in a SSNIP. The pre-merger benchmark price is the anticipated price in the absence of a merger – this could simply be the pre-merger price or a future price based on anticipated price change from innovation or product entry. Market participants include firms that currently earn revenues in the relevant product / geographic market, and may include firms that are committed to entering the market in the near future or could

⁴⁶ "Horizontal Merger Guidelines." U.S. Department of Justice & Federal Trade Commission. August 19, 2010. <http://www.justice.gov/atr/public/guidelines/hmg-2010.pdf>

⁴⁷ See Shapiro (1996); Farrell and Shapiro (2010).

enter rapidly without incurring significant sunk costs.⁴⁸ Market shares are based on actual or projected revenues in the relevant market.⁴⁹

Regarding market concentration, the FTC also examines the pre-merger concentration and the change in concentration resulting from the merger.⁵⁰ The FTC often calculates market concentration using the Herfindahl-Hirschman Index (“HHI”) – the sum of the squares of the individual firms’ market shares, which gives proportionately greater weight to the larger market shares. Concentration is generally categorized as follows: Unconcentrated markets (HHI < 1500); Moderately concentrated markets (1500 ≤ HHI ≤ 2500); Highly concentrated markets (HHI > 2500). Mergers that result in moderately concentrated markets with an increase of more than 100 HHI points and mergers that result in highly concentrated markets with an increase of between 100 and 200 HHI points both raise competitive concerns that result in further scrutiny by the FTC. Mergers that result in highly concentrated markets with an increase of more than 200 HHI points are subject to a rebuttable presumption of enhancing market power.

Mergers in the Pharmaceutical Industry

Although the US pharmaceutical market as a whole is unconcentrated, the product market definition used for on-patent drugs is usually the therapeutic class or indication, and at this level concentration can be a significant concern. In practice, most pharmaceutical cases appear to use traditional merger principles based on market shares, rather than attempting to measure cross-price elasticities. In horizontal mergers between large pharmaceutical firms, the FTC calculates changes in market concentration separately for each therapeutic area in the two firms’ combined product portfolio. This has often resulted in requirements that the merged firm divest products in overlapping therapeutic areas where the increase in concentration is deemed unacceptable. For example, in Pfizer’s acquisition of Wyeth, the FTC charged that the merger would reduce competition in 21 US markets for animal health products, that entry into these markets would not be timely or likely, increasing the likelihood of higher prices and harm to consumers. The consent order required Pfizer to divest the Fort Dodge US animal health products business in all areas of overlap to Boehringer Ingelheim Vetmedica, Inc., thereby preserving competition and strengthening a potential competitor.⁵¹

Market definition for on-patent products generally includes other molecules for the same indication that would be considered therapeutic substitutes. For off-patent products, the market is sometimes defined to include only the bioequivalent generics, since these are the originator brand’s closest substitutes and have a unique and potentially large competitive impact on the originator. Similarly, in the US the over-the-counter (OTC) market would generally be considered separate from the prescription drug market, because OTCs do not require a physician’s prescription, are generally less potent and are not covered by insurance, whereas prescription-bound (Rx) products are usually more

⁴⁸ “Horizontal Merger Guidelines.” U.S. Department of Justice & Federal Trade Commission. August 19, 2010. <http://www.justice.gov/atr/public/guidelines/hmg-2010.pdf>

⁴⁹ “Horizontal Merger Guidelines.” U.S. Department of Justice & Federal Trade Commission. August 19, 2010. <http://www.justice.gov/atr/public/guidelines/hmg-2010.pdf>

⁵⁰ “Horizontal Merger Guidelines.” U.S. Department of Justice & Federal Trade Commission. August 19, 2010. <http://www.justice.gov/atr/public/guidelines/hmg-2010.pdf>

⁵¹ “Complaint: In the Matter of Pfizer Inc. and Wyeth.” Federal Trade Commission. January 29, 2010. www.ftc.gov/os/caselist/0910053/index.shtm.

potent, are covered by insurance and have a higher total price (although the patient's copayment may be modest).⁵²

The following cases provide examples of the application of US merger principles to the pharmaceutical industry.

*Valeant Pharmaceutical's acquisition of Sanofi's Dermik unit*⁵³

At issue in this case were two off-patent products with generic equivalents. The FTC defined the relevant markets as those for the manufacture and sale of these two products, BenzaClin and Topical 5FU in the United States, and considered the effect of the proposed acquisition on number of competitors and market shares. Sanofi's Dermik marketed branded BenzaClin. Valeant, having the only ANDA for generic BenzaClin and having licensed it to Mylan, received royalties from Mylan on sales of generic BenzaClin. The market before the acquisition was split between Dermik's branded BenzaClin and Mylan's generic BenzaClin.

The market for Topical 5FU had 5 competitors pre-acquisition: (1) Valeant's branded Efudex; (2) Spear Pharmaceuticals' generic Efudex; (3) Taro Pharmaceuticals' generic Efudex; (4) Dermik's branded Carac; and (3) Allergan's branded Fluoroplex. Valeant's branded Efudex sales had been almost completely eroded by generic Efudex. Post-acquisition, Valeant would have a market share of over 50% of the Topical 5FU market.

The FTC argued that competitive entry was unlikely to counteract the anti-competitive effects of the merger for two reasons: (1) The markets were unattractive for new entrants because the markets were small; (2) The drug development and approval timeline prevents competitors from entering the market in time to prevent the anti-competitive effects of the merger.

The FTC therefore concluded that the post-merger Valeant would be able to exercise unilateral market power in both product markets and raise prices for consumers. The consent order entered into between the FTC and Valeant required Valeant to (1) Sell to Mylan all rights in generic BenzaClin; and (2) License to Mylan the rights to the authorized generic version of Efudex.

*Johnson & Johnson's (J&J) acquisition of Pfizer's Consumer Healthcare business*⁵⁴

The FTC defined the four relevant markets as those for the research, development, manufacture, and sale of OTC products in each therapeutic area: OTC H-2 blockers, OTC hydrocortisone anti-itch products, OTC nighttime sleep-aids, and OTC diaper rash treatments. Concentration measures included the HHI, number of firms and market shares, pre and post-acquisition. The results were similar in all four markets.

The market for OTC H-2 blockers was highly concentrated, based on its HHI index. J&J and Pfizer were the two largest suppliers of the four suppliers of OTC H-2 blocker products, and together would account for over 70% of sales with their Pepcid and Zantac products. The acquisition would leave J&J as the dominant supplier and significantly increase concentration in this market. The OTC hydrocortisone

⁵² Treating Rx and OTC as separate markets may be less appropriate in countries where the Rx-OTC distinction is more blurred because both are self-pay and both may be available in practice without a prescription. Even in the US, substitutability between Rx and OTC products may be greater in classes where the same OTCs were formerly on-patent, Rx products that have gone through a formal FDA-approved OTC switch e.g. some antihistamines.

⁵³ "Complaint: In the Matter of Valeant Pharmaceuticals International, Inc." <http://www.ftc.gov/os/caselist/1110215/111209valeantsanoficmpt.pdf>.

⁵⁴ "Complaint: In the Matter of Johnson & Johnson and Pfizer, Inc." Federal Trade Commission. January 19, 2007. <http://www.ftc.gov/os/caselist/0610220/0610220complaint.pdf>

anti-itch market was similarly highly concentrated. J&J and Pfizer were the only significant suppliers of branded OTC hydrocortisone anti-itch products in the U.S. Their Cortaid and Cortisone products accounted for 55% of sales in the total market. The acquisition would significantly increase concentration in this market, again leaving J&J as the dominant supplier.

J&J and Pfizer were also the two largest suppliers of OTC nighttime sleep-aid products, with a high HHI index and only four total firms in the market. Together, J&J and Pfizer accounted for 45% of sales pre-merger, and the acquisition would significantly increase concentration, leaving J&J as the dominant supplier. The OTC diaper rash treatments market was also a four firm market that was highly concentrated according to its HHI. J&J and Pfizer accounted for 50% of sales with their Balmex and Destin products. The acquisition would again significantly increase concentration and leave J&J as the dominant supplier.

The FTC argued that entry into any of these four markets would not be timely, likely, or sufficient to deter or counteract the anticompetitive effects of the acquisition because: (1) entry would require the investment of extremely high sunk costs, and (2) a new entrant would find it difficult to convince retailers to carry its products.

The FTC therefore determined that the merger would substantially lessen competition and create a monopoly by eliminating competition between J&J and Pfizer, increasing the ability of the merged firm to unilaterally increase prices, and reducing the merged firm's incentives to improve service or product quality. The consent order entered into between the FTC and J&J required: (1) the divestiture of Pfizer's Zantac assets to Boehringer; (2) the divestiture of Pfizer's Cortizone and Unisom sleep-aid products to Chattem; and (4) the divestiture of J&J's Balmex diaper rash treatment product to Chattem.

FTC vs. Lundbeck

In *Federal Trade Commission v. Lundbeck*, involving two on-patent products, the Eighth Circuit affirmed a District court finding that the two drugs were not in the same market, using cross-price elasticity of demand to define the market.⁵⁵ The FTC asserted that Lundbeck (then called Ovation) purchased the rights to Indocin IV from Merck in 2005 and then in 2006 purchased the rights to NeoProfen, which was awaiting FDA approval for PDA (patent ductus arteriosus), a life-threatening heart condition. The FTC complaint argued that Lundbeck feared that NeoProfen would take substantial sales from Indocin and that it acquired NeoProfen to eliminate the threat. After acquiring NeoProfen, Lundbeck raised the price of Indocin by 1,300%, and then launched NeoProfen at the same price. At the time of the complaint, Lundbeck had maintained prices at these levels for two years. The FTC's complaint charged that Lundbeck's acquisition of NeoProfen substantially raised prices, reduced competition and maintained its monopoly in PDA treatments in violation of the Clayton and FTC Acts. The complaint sought divestiture and disgorgement of unlawfully obtained profits. Based on the testimony of neonatologists and clinical pharmacists, the District court determined that there was a low cross-price elasticity of demand between the two products and thus the products were not in the same product market, based on the finding that "neonatologists 'ultimately determine the demand for Indocin IV and Neoprofen,' and that these treatment decisions are made 'without regard to price.'"

This counterintuitive outcome highlights the pitfalls of relying on cross-price elasticity of demand to define product markets, when patients'/physicians' price elasticities are undermined by insurance. The FTC argued for a broader measure of cross-elasticities, not focusing solely on price, and that the district court failed to consider the hypothetical pricing situation, had the two products been

⁵⁵ *FTC v. Lundbeck, Inc.* 650 F. 3d 1236 (8th Cir., 2011). See also Statement of Commissioner Rosch in *FTC vs. Lundbeck Inc.* Jan. 20 2012.

owned by different firms. This case illustrates the difficulty of identifying anti-competitive price effects of a merger when insurance and physician agency already make demand highly price-inelastic.

Mergers of Retail Pharmacies and Wholesalers

The FTC has carefully monitored chain growth in the retail pharmacy sector and blocked several proposed acquisitions on grounds of enhanced market power in geographic markets. For retail pharmacy, the relevant geographic market is defined as the urban area within the state. Acquisition by one pharmacy chain in a state of another chain operating in overlapping cities in the same state has been either blocked or approved subject to divestiture in areas of significant increase in concentration.⁵⁶ For example, JCPenney's acquisition of 190 pharmacies from Rite Aid, followed by the acquisition of Eckerd in North and South Carolina led to a consent order that included a requirement of divestiture of a specified number of stores to another chain, to ensure that the buyer could serve as a competitive pharmacy chain within a PBM's pharmacy network.

In 1998 the FTC successfully challenged two mergers involving the four largest drug wholesalers – McKesson merging with AmeriSource and Cardinal Health with Bergen Brunswick. If the mergers had gone through, the two surviving firms would have controlled 80% of the prescription drug wholesaling market nationwide.

3. Potential Competition Mergers

Potential competition mergers involve one competitor buying a company that is planning to enter its market, or a planned entrant buying a competitor in that market.⁵⁷ These acquisitions could prevent the actual increase in competition that would result from entry, and could eliminate the procompetitive effects that result when potential entry by an outside firm is a deterrent to price increases by existing firms. The FTC has challenged mergers between pharmaceutical companies where both firms are potential entrants as well as mergers where one firm is already in the market with an FDA approved drug and the second firm has a drug that is under review and will be a competitor once approved.

*Watson's acquisition of Arrow*⁵⁸

Arrow was one of three existing suppliers of generic cabergoline, a drug used to treat Parkinson's disease. Watson had FDA approval to sell generic cabergoline and was poised to enter the market within two years. The FTC argued that the proposed acquisition would eliminate the potential entry of Watson's product. Additionally, Watson was one of two generic suppliers of dronabinol, a drug used to treat nausea and vomiting caused by cancer and HIV therapy. A subsidiary of Arrow was in the process of developing a generic dronabinol product, and was one of a limited number of firms capable of marketing generic dronabinol in a sufficiently timely manner to have competitive impact. The FTC argued that the proposed acquisition would eliminate the likely entry of Arrow's dronabinol product. Citing that, "in generic markets, pricing is heavily influenced by the number of competitors in the market," the FTC required that Watson divest its generic cabergoline product to Impax and that Arrow divest its subsidiary and sell its U.S. marketing rights for generic dronabinol to Impax. This case illustrates the use of the molecule to define the market in the case of mergers involving generic competitors.

⁵⁶ J.C. Penney Company/Eckerd Corporation/Rite Aid. 123 FTC

⁵⁷ "An FTC Guide to Mergers: Competitive Effects." Federal Trade Commission.
http://www.ftc.gov/bc/antitrust/factsheets/FactSheet_Competitive.pdf

⁵⁸ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

*Pfizer's acquisition of Pharmacia*⁵⁹

Pharmacia was one of two firms with an extended release, overactive bladder (OAB) product, with Pfizer one of two companies best positioned to enter the market within the next two years and seeking FDA approval for its extended release OAB product. Due to the likelihood that Pfizer would delay the launch of its product as a result of the merger, the FTC required that Pfizer divest its extended release OAB-related products to Novartis AG. Additionally, Pfizer had 95% of the U.S. erectile dysfunction (ED) market and had a second generation Viagra-like product in development. Pharmacia was Pfizer's only significant potential competitor, with two products in clinical development. Pharmacia was required to divest all its rights for its developing products to Natestch and Neurocrine Biosciences, Inc.

*Barr's acquisition of Pliva*⁶⁰

The patent on the branded nimodipine product had expired and no generic versions were yet on the market. Barr and Pliva were the only companies seeking approval for generic nimodipine. The proposed acquisition of Pliva by Barr would have eliminated potential competition in the nimodipine market. The consent order therefore required either that Pliva divest its nimodipine assets to Banner or Barr divest its nimodipine assets to Cardinal.

4. Innovation Market Mergers

In 1995, the FTC and DOJ issued the Antitrust Guidelines for the Licensing of Intellectual Property. These guidelines defined "innovation markets" as markets consisting of "the research and development directed to particular new or improved goods or processes, and the close substitutes for that research and development."⁶¹ "Close substitutes" include "research and development efforts, technologies, and goods that significantly constrain the exercise of market power with respect to the relevant research and development..." The guidelines state that these innovation markets are an appropriate target for antitrust regulation when the ability to perform the relevant research and development is dependent on the specialized assets or characteristics of a particular firm. The guidelines also suggested a safe harbor from antitrust regulation when five potential innovators exist in the market. After the publication of the guidelines, the FTC routinely required divestiture or compulsory licensing of intellectual property in the case of innovation market mergers.

An example of the FTC's regulation of innovation market mergers was the merger of Ciba-Geigy and Sandoz.⁶² The FTC argued that "[t]he firms' combined position in gene therapy research was so dominant that other firms doing research in this area needed to enter into joint ventures or contract with either Ciba-Geigy or Sandoz in order to have any hope of commercializing their own research efforts," and that a combined entity would reduce overall research in the area. A consent order required the newly combined company, Novartis, to grant all requesters a non-exclusive license to certain gene therapy technologies, for which Novartis could receive an up-front payment of \$10,000 and 1-3% royalties on net sales; licenses for other technologies allowed Novartis greater flexibility in negotiating the terms.

⁵⁹ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁶⁰ "In the Matter of Barr Pharmaceuticals acquiring Pliva." Federal Trade Commission. December 2006. <http://www.ftc.gov/enforcement/cases-and-proceedings/cases/2006/12/barr-pharmaceuticals-inc-matter>

⁶¹ "Antitrust Regulation of Innovation Markets: Remarks of J. Thomas Rosch." Federal Trade Commission. February 5, 2009. <http://www.ftc.gov/speeches/rosch/090205innovationspeech.pdf>

⁶² "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

Another example involved the acquisition by Glaxo of Burroughs Wellcome. These two firms were furthest along in developing an oral drug to treat migraine.⁶³ Existing migraine treatments were only available as injectables and the FTC excluded these from the relevant market. The FTC's complaint alleged that the acquisition would eliminate competition between the firms in researching oral migraine remedies and increase Glaxo's unilateral ability to reduce R&D for these drugs. A consent order required the divestiture of Wellcome's R&D-related migraine assets, including patents, technology, manufacturing information, testing data, customer lists, and "inventory needed to complete all trials and studies required to obtain FDA approval."

As noted above, for licensing agreements that exceed \$70m. a recent rule extends the HSR notification requirement if the deal transfers "all commercially significant rights" to "any therapeutic area (or specific indication within a therapeutic area)" *even if the licensor retains manufacturing or other rights* (emphasis added). This rule so far applies only to the pharmaceutical industry, including biologics and *in vitro* diagnostics.⁶⁴

5. Vertical Mergers

The FTC has scrutinized vertical acquisition by three large pharmaceutical companies of three large pharmacy benefit managers (PBM's), in light of the potential for the manufacturer to favor its own drugs on the PBM's formularies, foreclose competitors and undermine the PBM's role in constraining manufacturer prices.⁶⁵ Consent orders entered into with Merck and Eli Lilly, regarding their acquisitions of the PBMs Medco and PCS, respectively, required the acquired PBMs to: maintain and disclose an open formulary (including all drugs); establish an independent Pharmacy and Therapeutics committee, to objectively evaluate drugs; and accept all discounts, rebates etc. offered by competitor manufacturers for inclusion in the open formulary. Although the FTC permitted the PBM acquisitions, subject to these and other restrictions, all three were subsequently sold or spun off at a loss. This suggests that in the view of markets and customers, ownership of PBMs by pharmaceutical companies was perceived to undermine their value as neutral intermediaries to control drug prices.

In 2007, CVS, a leading retail pharmacy chain and clinic provider, acquired Caremark, the leading PBM, without objection by the FTC. This was potentially surprising, because one important function of PBMs is to define preferred pharmacy networks for insured patients and control pharmacy dispensing fees and drug mark-ups. In 2009 the FTC began an investigation into CVS Caremark's business practices, in response to complaints from customers, pharmacists, labor unions and others, but a two year investigation was subsequently closed without any enforcement action on any of the antitrust allegations. Thus the FTC did not take issue with the business practices that are common in vertically integrated businesses and specifically those involving PBM-pharmacy relationships.⁶⁶

⁶³ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁶⁴ Cernak, Steve et al. "Expanded HSR Rules Require Reporting of Pharmaceutical Patent Exclusive Licenses, All Exclusive Deals Called "Potentially Reportable" By FTC." November 14, 2013. <http://www.natlawreview.com/article/expanded-hsr-rules-require-reporting-pharmaceutical-patent-exclusive-licenses-all-ex>

⁶⁵ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>. A formulary is a list of covered drugs with associated cost-sharing. Drugs on the "preferred" tier have lower patient co-payment and tend to gain market share from drugs on "non—preferred" tiers with higher co-payments.

⁶⁶ "FTC Closes Antitrust and Unfair Competition Investigation of CVS Caremark Post-merger Marketing Practices." Akin Gump. January 19, 2012.

Another challenged vertical acquisition involved Fresenius' acquisition of an exclusive sublicense from Daiichi Sankyo to manufacture and supply the intravenous iron drug Venofer to dialysis clinics.⁶⁷ The FTC argued that the acquisition would give Fresenius, the largest provider of dialysis services, the incentive and power to increase its Medicare reimbursement for Venofer. The resulting consent order limited Fresenius' ability to report high prices to increase its reimbursement, but was ultimately rendered moot by new reimbursement methodologies implemented by Medicare.

6. Other Monopolization Cases

Patent "Evergreening"

Originator companies have strong incentives to try to extend the patent protection on their products. The Hatch Waxman Act's Paragraph IV provision creates an incentive for generic firms to challenge patents that are potentially invalid, but also enabled originator firms to obtain a 30 month stay on the ANDA approval while the disputed patent is under litigation. Because there could be multiple, successive 30-month stays, originators had incentives to file patents for additional features or purified forms of their drugs, metabolites etc. When generic companies are sued for infringing such patents, they have sometimes claimed that these patents constitute attempted monopolization, in violation of Section 2 of the Sherman Act. Generic companies have sometimes succeeded in asserting a private antitrust action against such patents that harm their ability to compete.⁶⁸ However, this potential antitrust liability may be blocked by the originator's First Amendment right to petition for legislative, executive administrative or judicial action, under the Noerr Pennington doctrine, which generally protects the right to file patent infringement claims. Patents are generally presumed valid and the burden is on the challenger to demonstrate invalidity with clear and convincing evidence. Further, there are no guidelines restricting the listing of patents in the FDA Orange Book.

Antitrust liability for frivolous patenting and/or filing an infringement action based on such a patent requires either that (a) the patent was acquired through knowing and willful fraud, or (b) "the patent infringement suit ...was objectively baseless and subjectively motivated by a desire to impose collateral, anti-competitive injury rather than to obtain a justifiable legal remedy."⁶⁹ In *Bristol-Myers Squibb Co. v. Ben Venue Laboratories*, the District Court of New Jersey stated that "antitrust liability under Section 2 of the Sherman Act may arise when a patent has been procured by knowing and willful fraud, the patentee has market power in the relevant market, and has used its fraudulently obtained patent to restrain competition." The generic company must show that the patentee "1) knowingly and willfully made a fraudulent omission or misrepresentation; 2) with clear intent to deceive the patent examiner; [and] 3) the patent would not have issued but for the misrepresentation or omission."⁷⁰

The rulings on these late-filed patents have been mixed. FTC reviewed Eli Lilly's single isomer version of Prozac and found no antitrust violation. However courts have ruled that a patent on a metabolite does not apply to the drug,⁷¹ and that a generic does not infringe the patent on the

<http://www.akingump.com/en/news-publications/ftc-closes-antitrust-and-unfair-competition-investigation-of-cvs-caremark-post-merger.html>

⁶⁷ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁶⁸ *Bristol-Myers Squibb Co. v. Ben Venue Labs.*, 90 F. Supp. 2d 540, 543 (2000).

⁶⁹ C. Paine, "Brand-name drug manufacturers risk antitrust violations by slowing generic production through patent layering." *Seton Hall Law Review* 33:479.

⁷⁰ C. Paine, "Brand-name drug manufacturers risk antitrust violations by slowing generic production through patent layering." *Seton Hall Law Review* 33:479.

⁷¹ *Hoechst-Roussel Pharm., Inc.*, 109 F.3d at 759.

metabolite even though its active ingredient is converted into the metabolite in the body.⁷² Courts have also ruled against “obviousness-type double patenting,” that is, filing of additional patents that are not distinct from the original patents. Thus Eli Lilly’s second patent on Prozac, which would have extended Prozac’s monopoly for an additional three years, was successfully challenged by Barr Labs, arguing that the second patent simply showed the method by which the patented product worked.⁷³

Claims of monopolization are frequently joined by states attorneys general, claiming compensation for excessive costs to Medicaid and other state programs. For example, in March 2006, Glaxo Smith-Kline agreed to pay \$14m. to resolve allegations of charging inflated prices for Paxil, an anti-depressant drug, to state government programs, because GSK engaged in patent fraud, antitrust violations, and frivolous litigation to maintain a monopoly and prevent generics entering the market.⁷⁴

Product Hopping

“Product hopping” refers to the practice by an originator firm of making minor product reformulations that offer patients little or no therapeutic advantage, but effectively block generic competition simply because they are different. Typically, the originator manufacturer launches a new formulation of its product, such as a long-acting formulation, prior to patent expiry and generic entry on the original formulation. The originator then persuades physicians and patients to switch to the new formulation by raising the price of the original product above the reformulated product, switching all marketing efforts to the new formulation and sometimes removing the original formulation from the market. Because, under U.S. substitution laws, pharmacies may only substitute generic products of exactly the same formulation and strength as the patent-expired originator formulation, a reformulation and induced switching of prescriptions to the new formulation effectively blocks pharmacy substitution and thus eliminates meaningful generic competition. A generic producer could in theory invest in promotion to try to persuade physicians to prescribe its generic product; however, even if the prescription were written for a particular generic, pharmacies could substitute other generics which could sell at lower prices because they had not invested in promotion. Thus individual generics have no incentive to promote, under the pharmacy substitution rules that exist in the US, and most are unbranded, which reduces costs and contributes to low generic prices. An unintended consequence of generic substitutability is that the originator can block generics by withdrawing the reference product.

State Attorneys General have successfully prosecuted product hopping cases. For example, in January 2010 California and 23 other states won a \$22.5 million settlement with Abbott and Fournier, which used minor reformulations and filed frivolous patent suits to delay generic competition for the cholesterol-reducing drug, Tricor.⁷⁵

The FTC recently filed an amicus brief denouncing the practice of “product switching” or “product hopping”⁷⁶, although it has not yet been the challenging party in such a case. The case involved generic manufacturer Mylan suing Warner Chilcott, manufacturer of the originator product Doryx, for releasing three successive reformulations of Doryx that offered little or no therapeutic improvement to consumers, but successfully impeded meaningful generic competition and preserved Warner Chilcott’s monopoly profits. The FTC stated, in support of Mylan’s challenge that “a brand company can interfere with the mechanism by which generic drugs compete by making modest non-

⁷² *In re Omeprazole Patent Litig.*, No. 1291, 2001 U.S. Dist. LEXIS 7103, 1 (S.D.N.Y. May 29, 2001).

⁷³ *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 967 (Fed. Cir. 2001).

⁷⁴ “Pharmaceuticals.” State of California Department of Justice. <http://oag.ca.gov/antitrust/pharmaceuticals>.

⁷⁵ “Pharmaceuticals.” State of California Department of Justice. <http://oag.ca.gov/antitrust/pharmaceuticals>.

⁷⁶ Brief for the FTC as Amicus Curiae, *Mylan Pharmaceuticals, Inc. v. Warner Chilcott Public Limited Company*, Civil Action No. 12-3824 (E.D. Pa.) (November 21, 2012).

therapeutic changes to its product, and effectively prevent generic competition, not because the reformulated product is preferred by consumers, but simply because it is different.” Citing the fact that generic drugs rely on at-the-pharmacy substitution and not marketing to reach consumers, the FTC argued that generic manufacturers’ only response to product hopping would be to reformulate the generic product to match the reformulated branded product.

Acknowledging that product changes are often procompetitive, the FTC nonetheless stated that Warner Chilcott’s three reformulations offered little or no therapeutic benefit and therefore allowed the branded firm to “manipulate the FDA regulatory process and undermine state and federal laws that encourage generic competition,” and “preclude and/or reduce, rather than expand consumer choice.” The FTC challenged Warner’s presumption that product innovation is *per se* legal, arguing that any benefits of innovation should be weighed against any anti-competitive effects. Citing *US vs. Microsoft* the FTC states: “judicial deference to product innovation... does not mean that a monopolist’s product design decisions are *per se* lawful.” In this case the claimed innovations offered no therapeutic benefits but eliminated the benefits of generic competition, in violation of section 2 of the Sherman Act, which prohibits monopolization through means other than standard, commercial strategies, such as lower prices or product enhancement.

Commentary

In this US case, Warner’s patent on Doryx and its attempt to extend it via a new formulation with minimal incremental therapeutic value, were apparently sufficient to establish its monopoly and attempt to monopolize in violation of Sherman Section 2, without need to consider possible therapeutic substitutes for Doryx. This suggests that in the US product hopping that deters generic entry is potentially illegal for any originator drug, without regard to the availability of therapeutic substitutes in the class. When the issue is obstruction of generic competition, the FTC usually defines the market by the molecule rather than the therapeutic class, because generics are the closest substitutes. This is in contrast to a recent EU product hopping case against Astra Zenica, in which a key contended issue of fact was whether AZ’s product Losec had a dominant position in the market for omeprazole and similar products, which presumably would include other proton-pump inhibitors, such that withdrawal of Losec would constitute abuse of a dominant position. Thus in this EU case, having a patent was not sufficient to establish that AZ had a dominant position in the market for the molecule omeprazole (Losec); rather, the market was defined to include all proton-pump inhibitors. This is discussed in section V.4 below.⁷⁷

7. Illegal Tying and Other Arrangements

Illegal tying occurs when a monopolist uses forced buying through its market power to gain sales in markets where it is not dominant or make it more difficult for competitors to gain sales.⁷⁸ Such cases are rare in pharmaceuticals. In one exception, in 1992, the FTC entered into a consent order with Sandoz Pharmaceuticals regarding illegal tying. The FTC alleged that Sandoz illegally tied sales of its schizophrenia drug to distribution and patient-monitoring services and raised the price of the drug, which in turn reduced competition from other entities that provided the tied services. The consent order prohibited Sandoz from requiring such tying.

⁷⁷ Note that the FTC’s concern arises in part because generic approval and pharmacy substitution in the US require a reference product, hence replacement of the reference product by a new formulation can be a mechanism whereby the originator can block generic entry. The anticompetitive nature of new formulations may be less compelling in countries that permit regulatory approval and pharmacy substitution of similars, without the necessity of a reference product.

⁷⁸ “FTC Guide to the Antitrust Laws: Exclusionary or Predatory Acts: Tying the Sale of Two Products.” Federal Trade Commission. http://www.ftc.gov/bc/antitrust/tying_sale.shtm.

8. Agreements Not to Compete

Agreements among competitors not to compete may take many different forms. In pharmaceuticals, the most common case type scrutinized by the FTC is “pay-for-delay” settlements whereby originator firms and potential generic entrants agree to delay generic entry.⁷⁹ The incentives for such agreements are strong: delay of generic entry can prolong the period of sales at the monopoly price, which may be 5-10 fold higher than the market price after generic entry, with minimal difference in volume sold, enabling both parties to profit from the delay (see Section III.3 above).

Pay-for- Delay Settlements

Pay-for-delay settlements usually arise out of patent infringement suits brought by originator firms against generics that challenge their patents. Settlement of litigation is usually encouraged by the US judicial system. The FTC has challenged these cases when the settlement involves payment (in some form) by the originator to the generic, but not if the parties simply agree on an entry date for the generic that lies between its ANDA-approval date and the patent expiration date. In 2004, the Medicare Modernization Act (MMA) required that originator and generic drug manufacturers file certain agreements with the FTC and the Assistant Attorney General, including those regarding the manufacture, marketing, or sale of an originator drug for which an ANDA has been submitted, or the 180-day exclusivity period.⁸⁰ Lower court rulings have differed. In 2003 one appellate court held such agreements *per se* illegal.⁸¹ Since 2005, several appellate courts have upheld pay-for-delay agreements, and the number of such agreements has risen.⁸²

In 2012, the FTC reported the highest number of pay-for-delay settlements since the agency started collecting such data in 2004. (It is unclear whether this reflects an increase in the frequency of pay-for-delay cases per patent expiry/challenge or simply an increase in the number of patent expiries, or possibly a broader definition of payment⁸³). Specifically, in FY2012 the FTC received 140 final resolutions of patent disputes between an originator and generic. The FTC categorized 40 of these resolutions as “potentially pay-for-delay” – they contain both a “payment” to the generic manufacturer and a restriction on the generic manufacturer’s entry to market a product.⁸⁴ The FTC uses a definition of “payment” that includes not only direct monetary payment, but also other types of consideration that involve transfer of value from the originator to the generic firm. The key issues used by the FTC in deciding whether a settlement involves reverse payment are: 1. Is the alleged payment something that the generic challenger could not have obtained, had it won the litigation, and 2. Are the parties sharing monopoly profits preserved by avoiding competition?⁸⁵ Thus a settlement where the parties simply

⁷⁹ “Overview of Antitrust Actions in Pharmaceutical Services and Products.” Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁸⁰ “Medicare Prescription Drug and Improvement Act Requires Drug Companies to File Certain Agreements with the Federal Trade Commission and U.S. Department of Justice.” Federal Trade Commission. January 2004. <http://www.ftc.gov/os/2004/01/040106pharmrules.pdf>.

⁸¹ FTC (2010). Pay-for-delay.

⁸² FTC (2010). Pay-for-delay.

⁸³ “Antitrust Alert: New FTC Pharma Patent Litigation Report Finds Increase in ‘Reverse Payment’ Settlements Based on Expanded Definition of ‘Payments.’” Jones Day. February 2013. <http://www.jonesday.com/Antitrust-Alert--New-FTC-Pharma-Patent-Litigation-Report-Finds-Increase-in-Reverse-Payment-Settlements-Based-on-Expanded-Definition-of-Payments-02-06-2013/?RSS=true>.

⁸⁴ “Agreements Filed with the Federal Trade Commission under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003: Overview of Agreements Filed in FY 2012” Federal Trade Commission. <http://www.ftc.gov/os/2013/01/130117mmareport.pdf>.

⁸⁵ FTC Amicus Brief in Effexor XR Antitrust Litigation, http://www.ftc.gov/sites/default/files/documents/amicus_briefs/re-effexor-xr-antitrustlitigation/

agree on a date for generic entry after ANDA approval but before patent expiration would likely be considered simply a bargaining compromise and not subject to antitrust challenge.

In a recent pay-for-delay case brought by the FTC, the US Supreme Court ruled that a pay-for-delay patent settlement is not immune from antitrust scrutiny, even if its anticompetitive effects are within the scope of the exclusionary potential of the patent.⁸⁶ The FTC's original complaint challenged agreements in which the originator firm, Solvay, paid generic drug makers, Actavis (previously known as Watson Pharmaceuticals) and Paddock (affiliated with Par), to delay generic competition to Solvay's testosterone-replacement drug AndroGel.⁸⁷ Actavis and Paddock both sought FDA approval to market generic versions of AndroGel, which was Solvay's bestselling product.⁸⁸ In filings with the FDA, both generic firms stated that their products did not infringe on Solvay's patent and that the patent, set to expire in August 2020, was invalid.⁸⁹ Actavis received FDA approval to market its generic product in 2006. Solvay initiated patent litigation against the generic firms, which ultimately ended in a settlement in 2006.⁹⁰ Under this settlement, Solvay paid Actavis and Paddock substantial sums, conditioned on the generic firms' delaying generic entry until 2015 and abandoning their patent challenges.⁹¹ Additionally, Actavis entered into a marketing agreement with Solvay, through which it would be paid millions of dollars to promote AndroGel to urologists.⁹² The FTC challenged these agreements, charging that the three firms were cooperating on AndroGel sales and sharing monopoly profits, harming competition through the elimination of the two potential generic competitors, and that consumers were harmed by being forced to pay higher prices than if generic versions were available.⁹³ The Eleventh Circuit had affirmed dismissal of the FTC's complaint, on grounds that an agreement is immune from anti-trust attack if its anti-competitive effects are "within the scope of the exclusionary potential of the patent."⁹⁴ The Supreme Court reversed, rejecting this so-called "scope of the patent" approach, explaining that its longstanding approach to assessing agreements between a patentee and its potential competitors considers "traditional antitrust factors such as likely anti-competitive effects, redeeming virtues, market power, and potentially offsetting legal considerations...such as here those related to patents."⁹⁵

The Supreme Court noted that the antitrust concern with reverse payments is that "The payment's objective is to maintain supracompetitive prices to be shared among the patentee and the patent challenger rather than face what might have been a competitive market."⁹⁶

However, the Supreme Court stopped short of finding that all pay for delay settlements should be *per se* illegal or even subject to a "quick look" analysis, which would shift the burden of proof of

130816effexoramicusbrief.pdf.

⁸⁶ *FTC v. Actavis*, No. 12-416, 570 U.S. ___ (June 17, 2013).

⁸⁷ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁸⁸ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁸⁹ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁹⁰ *FTC v. Actavis*, No. 12-416, 570 U.S. ___ (June 17, 2013).

⁹¹ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁹² *FTC v. Actavis*, No. 12-416, 570 U.S. ___ (June 17, 2013).

⁹³ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

⁹⁴ *Actavis*, 133 S.Ct. at 2227, quoting *FTC v. Watson Pharms.Inc.*, 677 F3d 1298, 1312 (11thCir.2012)

⁹⁵ *Id.* at 2231.

⁹⁶ *Id.* at 2235.

legality to the defendant. Rather, the Supreme Court held that reverse settlement agreements must undergo “rule-of-reason” analysis, to consider “the likelihood of a reverse payment bringing about anticompetitive effects depends upon its size, its scale in relation to the payor’s anticipated future litigation costs, its independence from other services for which it might represent payment, and the lack of any other convincing justification.”⁹⁷ Thus going forward the legality of these pay-for-delay settlements will hinge on the magnitude and reasonableness of the payment.

States Attorneys General have also successfully challenged agreements between originator and generic companies to delay generic entry, resulting in higher drug costs to state-run health programs. Some of these cases have resulted in large payments to states and compensation for attorney fees.⁹⁸

Agreements on Price or Price-Related Terms

Agreements among competitors that fix prices are *per se* illegal. However collaborations among competitors that involve price agreements are subject to a rule of reason analysis, if the participants share financial risk or are clinically integrated and the pricing agreement is necessary to achieve integration efficiencies.⁹⁹ In the US, the FTC generally refers price fixing matters to the DOJ for possible criminal prosecution. Such cases may also be brought by private parties.

Actions by antitrust authorities alleging price fixing by manufacturers of originator prescription drugs are rare. As argued above, this may reflect the price-inelastic demand for many on-patent prescription drugs due to insurance coverage, physician agency and product differentiation. Inelastic demand enables high prices even in the absence of collusion. Firms compete through promotion to physicians and patients of brand and product attributes, not price. Moreover, the confidentiality of rebates that firms give to payers and PBMs has been maintained, despite some pressures for transparency, because confidentiality makes collusive agreements harder to maintain.¹⁰⁰

The international vitamins cartel that operated from 1989 to 1999 and involved producers in the EU, Japan and the US is one example of a major price-fixing case that applied to OTC products, although some of the firms involved also supply prescription pharmaceuticals.¹⁰¹ The case resulted in a fine of 855million Euros in the EU, and additional fines in the US, Canada and Australia. It is notable that vitamins are OTC products that are not generally reimbursed by insurance. Thus consumer demand is more price-elastic and potential gains from collusion would be higher than for reimbursed drugs. Moreover, because OTC products are not reimbursed, powerful payers play no role in regulating or negotiating prices on behalf of consumers, in contrast to prescription pharmaceuticals. It is thus unsurprising that this OTC sector has been more prone to price collusion than the prescription drug sector in countries with insurance coverage for prescription drugs. More recently, in a 2013 private civil class action case, a New York jury found Chinese Vitamin C manufacturers liable for price fixing, rejecting the defense that the agreement was compelled by the Chinese government. The jury awarded \$54m.

⁹⁷ FTC v. Actavis, No. 12-416, 570 U.S. __ (June 17, 2013).

⁹⁸ “Pharmaceuticals.” State of California Department of Justice. <http://oag.ca.gov/antitrust/pharmaceuticals>.

⁹⁹ FTC/DOJ Antitrust Guidelines for Collaborations Among Competitors, available at <http://www.ftc.gov/sites/default/files/attachments/press-releases/ftc-doj-issue-antitrustguidelines-collaborations-among-competitors/ftcdojguidelines.pdf> and the Health Care Statements, available at http://www.ftc.gov/sites/default/files/attachments/competition/policyguidance/statements_of_antitrust_enforcement_policy_in_health_care_august_1996.pdf.

¹⁰⁰ Stigler, G. “The Theory of Oligopoly” *The Journal of Political Economy*, Vol. 72, Issue 1 (Feb. 1964), 44-61. Outlines market conditions that make oligopolistic agreements hard to sustain.

¹⁰¹ Clarke, J.L. and Evenett, S.J. 2003. “The deterrent effects of national anticartel laws: evidence from the international vitamins cartel.” *Antitrust Bulletin* 48(3):689-726.

damages which, by law, was tripled to \$162m.¹⁰² The plaintiffs in this case were American food and beverage companies, and wholesalers and distributors of vitamins.

The FTC has challenged pricing agreements in other areas of health care, notably price agreements among physicians. In the pharmaceutical industry FTC-initiated actions challenging agreements on price have occurred mainly to agreements between pharmacies to fix contract prices charged to insurers and pharmacy benefit managers (PBMs).¹⁰³ A recent case involved Cooperativa de Farmacias Puertorriquenas (Coopharma), a cooperative representing at least one-third of pharmacies in Puerto Rico. The FTC alleged that the facilitation of agreements by Coopharma and the threat of collective action by Coopharma's pharmacies led insurers to pay the group's members higher rates. A consent order entered into in 2012 prohibited Coopharma from facilitating agreements with insurers on behalf of its member pharmacies or encouraging information exchange between pharmacies regarding whether to contract with a payer.

In Institutional Pharmacy Network (IPN), a similar case involving institutional pharmacies that cooperated to collectively offer their services to long term care institutions, the FTC argued that the pharmacies formed IPN to maximize their leverage in bargaining over reimbursement rates, but did not share risk or provide new or efficient services. The consent order prohibits IPN and the pharmacy respondents from entering into joint negotiations or agreements on price.¹⁰⁴ But it permits IPN to engage in conduct that is reasonably necessary to share financial risk or clinically integrate to achieve efficiencies.

Anti-competitive agreements have occasionally occurred in the supply of generics. In particular, in July 2000 the FTC and 32 states obtained injunctive relief and a \$100 million settlement payment from Mylan and another API producer and its parent company and distributor, that allegedly monopolized, attempted to monopolize, and conspired to monopolize the market for two anti-anxiety medications, lorazepam and clorazepate, by refusing to sell the active ingredients (APIs) to competitors. After entering into exclusive licensing agreements that deprived competitors of the APIs for the two drugs, Mylan increased prices 1,900 to over 3,200 percent, depending on the bottle size and tablet strength, and agreed to share profits with the other three companies.¹⁰⁵ The FTC settlement of \$100m., which also resolved the States' claims, was the largest settlement in FTC history at that time. Together with a separate payment to certain private plaintiffs, Mylan's payments were estimated to equal all profits from the challenged activities.

9. Price discrimination

Private suits alleging agreement on price and price discrimination by drug manufacturers have been initiated by pharmacies and other customers. In 1993, a class action lawsuit by retail pharmacies

¹⁰² <http://www.dlapiper.com/en/us/insights/publications/2013/06/chinese-vitamin-c-manufacturers-found-liable-for/> (last accessed 4.4.2014)

¹⁰³ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

¹⁰⁴ "Overview of Antitrust Actions in Pharmaceutical Services and Products." Federal Trade Commission. March 2013. <http://www.ftc.gov/bc/healthcare/antitrust/rxupdate.pdf>

¹⁰⁵ *FTC v. Mylan Laboratories, In., Cambrex Corporation, Profarmaco SRI and Gyma Laboratories of America, Inc.* 2000, accessed at <http://www.ftc.gov/enforcement/cases-proceedings/9810146/mylan-laboratories-inc-cambrex-corporation-profarmaco-sri-gyma>. Also "Pharmaceuticals." State of California Department of Justice. <http://oag.ca.gov/antitrust/pharmaceuticals>.

was instituted against several pharmaceutical manufacturers, seeking damages and an injunction for the manufacturers' practice of charging retail pharmacies much higher prices than HMOs and other 'favored' customers, including PBMs.¹⁰⁶ In 1998, this suit was settled for \$345 million by four pharmaceutical companies; the drug makers also agreed to refrain from a two-tier pricing system.¹⁰⁷ However, although the manufacturers agreed to offer the same price terms to similarly situated customers, in fact PBMs and HMOs are able to use their formulary design to influence utilization and market shares of on-patent drugs, whereas pharmacies are only legally permitted to do generic substitution. Thus PBMs and health plans that can influence market share of originator products through formulary design continue to receive larger discounts on on-patent drugs, in return for increased market share, compared to retail pharmacies that can only substitute between generics.

More recently, in 2012, in *Drug Mart Pharmacy Corp. v. American Home Products Corp.*, a judge granted summary judgment in favor of pharmaceutical manufacturers on a price fixing lawsuit brought by retail pharmacies. The pharmacies sued the drug manufacturers for illegal price-fixing under the Robinson-Patman Act. Under the Act, the plaintiff must establish that: "(1) the seller's sales were made in interstate commerce; (2) the seller discriminated in price as between the two purchasers; (3) the product or commodity sold to the competing purchasers was of the same grade and quality; and (4) the price discrimination had a prohibited effect on competition."¹⁰⁸ Despite there being a disparity in pricing between the plaintiffs and "favored pharmacies," the plaintiffs were unable to show an injury that was more than "de minimis" – "[m]any pharmacies lost no more than ten customers per defendant over the relevant twelve-year time period, or less than one customer per year."¹⁰⁹

Proving harm to competition, as required by the Robinson-Patman Act, as opposed to harm to individual competitors, is frequently problematic for plaintiffs in price discrimination cases. Such cases are often brought by customers that do not receive the same discounts as other, "favored" customers. But if the favored customers pass on the discounts to patients and gain in market share, there is likely no harm to competition, even though individual competitors may lose share. Similarly, private claims challenging PBM relationships as exclusive dealing or boycotts have generally been unsuccessful. Challenges to PBM pricing under the Robinson Patman Act have also been rejected.¹¹⁰

V. Antitrust Policy in the EU

1. Antitrust Law

The EU antitrust policy as set out in the Treaty on the Functioning of the European Union (TFEU) is founded on two basic Articles as follows:¹¹¹

¹⁰⁶ "Stores Sue Makers Of Drugs A Group Of Pharmacies Is Charging Price-fixing. They Say Retailers Pay Up To 12 Times More Than Other Buyers." Philly.com. October 15, 1993. http://articles.philly.com/1993-10-15/news/25938665_1_schering-plough-major-drug-manufacturers-pharmacies-charge.

¹⁰⁷ Morrow, D. "4 Drugs Makers Move to Settle In Pricing Suit." *New York Times* July 15, 1998 <http://www.nytimes.com/1998/07/15/business/4-drug-makers-move-to-settle-in-pricing-suit.html> Accessed November 2013 online.

¹⁰⁸ *George Haug Co. v. Rolls Royce Motor Cars Inc.*, 148 F.3d 136, 141 (2d Cir.1998).

¹⁰⁹ *Drug Mart Pharmacy Corp. v. Am. Home Products Corp.*, 93-CV-5148 ILG, 2012 WL 3544771 (E.D.N.Y. Aug. 16, 2012)

¹¹⁰ Antitrust Law Developments (Seventh) Volume II. American Bar Association ed. J.I Glecken. P. 1451ff.

¹¹¹ Consolidated version of the Treaty on the Functioning of the European Union - PART THREE: UNION POLICIES AND INTERNAL ACTIONS - TITLE VII: COMMON RULES ON COMPETITION, TAXATION AND APPROXIMATION OF

Article 101 (formerly Article 81 TEC) prohibits agreements that restrict competition:

1. The following shall be prohibited as incompatible with the internal market: all agreements between undertakings, decisions by associations of undertakings and concerted practices which may affect trade between Member States and which have as their object or effect the prevention, restriction or distortion of competition within the internal market, and in particular those which:

(a) directly or indirectly fix purchase or selling prices or any other trading conditions;
(b) limit or control production, markets, technical development, or investment;(c) share markets or sources of supply;(d) apply dissimilar conditions to equivalent transactions with other trading parties, thereby placing them at a competitive disadvantage; (e) make the conclusion of contracts subject to acceptance by the other parties of supplementary obligations which, by their nature or according to commercial usage, have no connection with the subject of such contracts.

2. Any agreements or decisions prohibited pursuant to this Article shall be automatically void.

3. The provisions of paragraph 1 may, however, be declared inapplicable in the case of:

- any agreement or category of agreements between undertakings,
- any decision or category of decisions by associations of undertakings,
- any concerted practice or category of concerted practices, which contributes to improving the production or distribution of goods or to promoting technical or economic progress, while allowing consumers a fair share of the resulting benefit, and which does not:

(a) impose on the undertakings concerned restrictions which are not indispensable to the attainment of these objectives; or
(b) afford such undertakings the possibility of eliminating competition in respect of a substantial part of the products in question.

Article 102 (formerly Article 82 TEC) prohibits firms in a dominant position from abusing their dominant position, unless such conduct can be objectively justified:

Any abuse by one or more undertakings of a dominant position within the internal market or in a substantial part of it shall be prohibited as incompatible with the internal market in so far as it may affect trade between Member States. Such abuse may, in particular, consist in:

(a) directly or indirectly imposing unfair purchase or selling prices or other unfair trading conditions;
(b) limiting production, markets or technical development to the prejudice of consumers;
(c) applying dissimilar conditions to equivalent transactions with other trading parties, thereby placing them at a competitive disadvantage;
(d) making the conclusion of contracts subject to acceptance by the other parties of supplementary obligations which, by their nature or according to commercial usage, have no connection with the subject of such contracts.

In summary, Article 101 prohibits agreements between two or more independent market operators that harm competition, including both horizontal and vertical agreements. Article 102 prohibits firms that hold a dominant position from abusing that position, for example, by charging unfair prices, limiting production in ways that harm consumers, price discrimination or tying arrangements.¹¹²

Additionally, the EU Merger Regulations (EUMR) require pre-notification to the EC of mergers and joint ventures where the annual turnovers of the firms involved exceed certain thresholds, if the parties do business in the EU, regardless of their countries of domicile. Below these thresholds, national competition authorities may review merger and JV transactions.

Articles 107 to 109 TFEU preclude national authorities from conferring advantages to firms on a selective basis.

Enforcement is by the EU Commission, in cooperation with the National Competition Authorities (NCAs) of member states, through the European Competition Network. The NCAs retain the right to establish their own competition law for activities that are domestic only, but EU law applies to any activity that affects interstate commerce or other EU member states. The EU Courts have generally limited themselves to verifying whether the Commission has acted lawfully, and have generally granted the Commission substantial discretion in the economic analysis of facts.¹¹³ Private actions for damages for breach of competition law are permitted.

The EU Directorate General for Competition (DG Competition) monitors business practices, company mergers and state aid in the health care sector. In July 2010 it integrated its antitrust activities regarding all health care sectors in a new unit called "Antitrust: Pharma and Health services", responsible for competition law enforcement for all health products and services.

Market definition

As in the US, market definition in the EU has both a product and a geographic element. Product market definition relies primarily on demand-side substitutability, but supply-side substitutability and potential competition may also be relevant. Demand-side substitutability is measured through the use of a "small but significant nontransitory increase in price" test (SSNIP test). If a 5-10% change in price would lead customers to switch to the lower-priced product, the products are substitutable. A similar test is applied to determine geographic substitutes.

Parallel Trade

Parallel trade (the commercial importation of drugs by third parties, without the patent-holder's permission) is permitted between EU member states, under the Treaty of Rome, but importation from outside the EU is not permitted. Drug prices sometimes differ significantly between EU member states, due to differences in regulatory systems, per capita income, etc., which creates the opportunity for price arbitrage by distributors. The EU Commission views parallel trade as a valid form of competition. Parallel trade cases have sometimes raised antitrust issues.

2. Application to the Pharmaceutical Industry

The EU Commission recognizes that the market for medicines is heavily and differently regulated in each member country, which leaves less room for price competition than in most other sectors.

¹¹² "Antitrust." European Commission. August 16, 2012.

http://ec.europa.eu/competition/antitrust/overview_en.html

¹¹³ Fanelli, M. J. et al. Competition laws outside the United States. Chicago: Section of Antitrust Law, American Bar Association, c2011. Print.

Further, patent protection for originator molecules means that competition between them is more in areas of innovation than prices.¹¹⁴ However, once patents expire there is great potential for generic entry, price reductions and savings for consumers. Barriers to competitive entry, through parallel trade and generics, has been a major focus of competition policy.

Parallel Trade

Originator firms have adopted many strategies to deter parallel trade, including launch timing, differential packaging, and limiting supplies to national wholesalers. These are generally unilateral actions that are legal, even if they have the effect of raising costs of parallel traders.

In *Bayer v. Commission*,¹¹⁵ the European Court of Justice (ECJ) upheld the General Court's (GC) annulment of the Commission's decision that fined Bayer for limiting the supply of Adalat to wholesalers who were engaged in parallel trade. The ECJ and GC took the view that Bayer's conduct was unilateral because it was not part of a contractual agreement between the two parties. If Bayer had required the wholesalers to restrict exports as a condition of doing business, this would have been an agreement and in violation of Article 101. But in this case there was no evidence that Bayer prevented the wholesalers from exporting the supplies of Adalat that they were allocated. Bayer's supply restriction was therefore deemed a unilateral action, not an agreement, and was not in violation of competition law.

Strategies to Delay Generic Entry: The Pharmaceutical Sector Inquiry (2008)

A major focus of EU Commission's antitrust concern in the pharmaceutical sector has been barriers to generic competition. The Pharmaceutical Sector Inquiry was initiated by the European Commission (EC) in 2008, following dawn raids on several pharmaceutical and generic companies, in response to concerns over delay in generic entry and decline in the number of novel medicines brought to market.¹¹⁶ The 2009 Preliminary Report provides a factual account of the Inquiry's findings for the period 2000-2007, based on analysis of 219 medicines. It does not attempt to reach conclusions as to whether certain practices described infringe EC competition law.

The Preliminary Report concludes that generic entry increases European patients' access to drugs and reduces national healthcare spending.¹¹⁷ However, the Report finds that generic entry is often delayed well beyond what would be expected based on the length of market exclusivity – on average, generics entered the market more than seven months after the originator medicines lost exclusivity, costing health systems 3 billion euros.¹¹⁸

The Inquiry identified five strategies used by originator companies to delay generic entry: (1) strategic patenting; (2) patent disputes and litigation; (3) patent settlements; (4) interventions before national regulatory authorities; and (5) life cycle strategies for follow-on products.¹¹⁹ Originators use these strategies most frequently for the best-selling medicines. Such strategic targeting makes sense if

¹¹⁴ "Pharmaceuticals and Health Services." European Commission. November 28, 2012.

http://ec.europa.eu/competition/sectors/pharmaceuticals/overview_en.html.

¹¹⁵ Case T-41/96, 2004 ECR. II-3383.

¹¹⁶ "Antitrust: Shortcomings in Pharmaceutical Sector Require Further Action – Frequently Asked Questions." July 8, 2009. http://europa.eu/rapid/press-release_MEMO-09-321_en.htm

¹¹⁷ "Pharmaceutical Sector Inquiry – Preliminary Report: Prices, Time to Generic Entry and Consumer Savings." European Commission. http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/fact_sheet_1.pdf

¹¹⁸ The Preliminary Report defines the "expected" date of generic entry based on termination of the originator's market exclusivity. It is unclear whether this includes regulatory exclusivity, primary and/or secondary patents.

¹¹⁹ "Pharmaceutical Sector Inquiry – Preliminary Report: Originator-Generic Competition." European Commission. http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/fact_sheet_2.pdf

litigation costs are largely invariant to the value of product litigated, such that the expected return on litigation increases directly with the value of the product, *ceteris paribus*.

Strategic Patenting

The Inquiry found that originator firms file multiple patents (“patent clusters or thickets”) on individual medicines, including many that are filed late in the product’s life cycle. Strategic patenting hinders generic entry by adding costs, uncertainty and delay related to patent challenges or waiting for patent expiry on all the patents. These costs are exacerbated in the EU because patent administration is national. Delay in generic entry leads to higher costs of medicines for consumers and payers. Defensive patenting can also block the development of new originator products, leading to delays and costs of negotiating and paying royalty payments.¹²⁰

Litigation

The Inquiry analyzed a sample of 219 medicines that were associated with over 1,300 patent-related out-of-court contacts and disputes, mostly initiated by originator companies, e.g. warning letters regarding their patents. These medicines were also associated with almost 700 cases of reported patent litigation related to 68 medicines. The majority of court cases were initiated by originator companies, but generic companies won the majority of cases (62%) where a final judgment was reached (149 cases). The average duration of patent litigation was 2.8 years. Because of the existence of national patent systems, in 30% of the cases studied, litigation occurred between the same parties in different EU Member States. Interim injunctions were granted in 112 of 225 cases where they were requested between 2000 and 2007 – these injunctions lasted, on average, 18 months. However, in 46% of the cases in which interim injunctions were granted, the generic company ultimately secured a favorable judgment or settlement.

The Inquiry identified more than 200 patent settlement agreements on 49 medicines between 2000 and 2008. In 48% of these cases, the generic company’s ability to market its medicine was restricted in exchange for some consideration from the originator to the generic company, either a direct payment, a license, distribution agreement or “side-deal.”

The pharmaceutical sector also has a relatively high rate of oppositions to patents filed with the European Patent Office (EPO). Generic companies almost exclusively opposed secondary patents. They prevailed in about 75% of final decisions rendered by the EPO but in 80% of cases resolving the dispute took more than 2 years. This finding of a higher generic challenge and win rate for secondary patents in the EU is consistent with evidence from analysis of US patent challenges, that generics win a much higher rate of challenges to secondary patents compared to primary, composition-of-matter patents.¹²¹

Interventions Before National Regulatory Authorities

The Inquiry determined that interventions by originator companies before national regulatory authorities – for example, arguing that marketing authorizations for generics violate their patent rights or that the generics were less safe or efficacious than the originator medicine – delayed marketing authorization of the generic by, on average, 4 months. Even this modest delay can result in significant costs to payers and patients, because originator delay efforts tend to focus on the highest valued medicines.

¹²⁰ “Pharmaceutical Sector Inquiry – Preliminary Report Executive Summary.” European Commission. November 28, 2008. http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/exec_summary_en.pdf

¹²¹ Mulcahy, A. (2011). *Patent policy and entry: Evidence from pharmaceutical patent challenges*. (Doctoral Dissertation). Retrieved from ProQuest Dissertations and Theses. (ProQuest document ID 878682730).

Life Cycle Strategies for Follow-on Products

The Inquiry determined that originator companies' switching patients to a follow-on product prior to the expiration of the first generation originator medicine's marketing exclusivity can inhibit generics for that first generation originator medicine from gaining market share. The first generation product is often withdrawn, which undermines substitution by pharmacies, which is usually permitted only within the same medicine and formulation. Obtaining a new patent or some regulatory exclusivity on the follow-on product facilitates this originator strategy. This raises difficult trade-offs for patent and competition authorities: although some follow-on products offer significant incremental innovation, the value of many incremental improvements is modest and must be weighed against any loss of savings from generic versions of the older product.

Strategic Patenting to Block Competitor R&D

The Inquiry also highlighted as anti-competitive certain unilateral practices of dominant companies, such as filing patents for areas that are related to but different from the areas they plan to pursue in their own R&D. By putting such information in the public domain, this strategic patenting blocks patenting by competitors and/or requires competitors to negotiate and pay a license fee, which discourages competitive R&D.

Recommendations of the Inquiry

The final Report recommended several policy changes, including the creation of a unified EU patent system and specialized review mechanism, and legislation to facilitate speedy launch of generics, including immediate pricing and reimbursement mechanisms for generics.¹²² The Report also recommended stronger scrutiny of the pharmaceutical industry by EU antitrust law, and ongoing monitoring of settlements between originators and generics, specifically the pay-for-delay settlements whereby the originator transfers value to the generic in return for delay in generic entry. Such settlements are viewed as restricting competition in exchange for sharing the monopoly rents.

Enforcement Action since the Pharmaceutical Inquiry

The EC has issued annual reports on its patent monitoring activities, in particular, pay-for-delay settlements that are potentially problematic from an antitrust perspective because they limit generic entry in return for a value transfer from an originator to one or more generic companies. These reports have concluded that while the number of settlements has increased, the proportion of settlements that may be problematic has fallen, from around 21% in the Inquiry to 11% in the 2012 report. This suggests that the EC monitoring has not deterred companies from entering into such settlements, contrary to fears expressed by some stakeholders, but that the monitoring may have increased stakeholders' awareness of anticompetitive potential.¹²³

The EC has sent a Statement of Objections to over 14 companies in several major cases. A Statement of Objections is a formal step in Commission investigations into suspected violations of EU antitrust rules. The Commission informs the parties concerned in writing of the objections raised against them and the companies can examine the documents on the Commission's investigation file, reply in writing and request an oral hearing to present their comments on the case before representatives of the Commission and national competition authorities. If, after the parties have exercised their rights of defense, the Commission concludes that there is sufficient evidence of an

¹²² "Antitrust: Shortcomings in Pharmaceutical Sector Require Further Action – Frequently Asked Questions." July 8, 2009. http://europa.eu/rapid/press-release_MEMO-09-321_en.htm

¹²³ "Antitrust: Commission enforcement action in pharmaceutical sector following sector inquiry." European Commission. http://europa.eu/rapid/press-release_MEMO-13-56_en.htm

infringement, it can issue a decision prohibiting the conduct and impose a fine of up to 10% of a company's annual worldwide turnover.

In the Citalopram case, in June 2013 the European Commission fined Lundbeck €93.8 million and several generic companies €52.2 million (including Alpharma, Arrow, Ranbaxy, Merck KGaA/Generics UK) over agreements that delay the market entry of generic citalopram.¹²⁴ The Commission concluded that such agreements violated Article 101 of the EU Treaty. At the time of the agreement, Lundbeck's basic patent for the citalopram molecule had expired. It still held related process patents that the Commission argued could have provided more limited protection, such that generics could have entered the market immediately.¹²⁵ In 2002, generic manufacturers agreed not to enter the market with generic citalopram in exchange for substantial value transfers, including lump sums, purchases of generics' stock by Lundbeck for the sole purpose of destruction, and guaranteed profits in a distribution agreement. Lundbeck has appealed to the General Court of the EU, and further appeal to the EU Court of Justice is possible, which may take several years.¹²⁶

The Perindopril case involved similar payments by originator Servier to several generic companies to not enter the market and not further challenge the validity of Servier's remaining patents. In the Fentanyl case, Sandoz refrained from launching a generic in the Dutch market and instead entered into a "co-promotion" agreement with originator J&J, which involved monthly payments by J&J to Sandoz as long as no generic product was launched. The agreement ceased when another firm launched a generic. The EU Commission imposed fines on J&J of €10.8m. and €5.5m. on Sandoz.

Commentary

These cases reveal complex and long term arrangements between a single originator and multiple generic firms. This suggests that entry barriers are high enough that originators do have incentives to pay multiple generics not to enter, and the risk of simply attracting other entrants does not make this strategy prohibitively costly, at least for high valued drugs. Although not explicitly discussed, the EC appears to consider the facts of each case and has not proposed using either a *per se* illegality rule or a scope-of-the-patent defense for these cases.

3. Abuse of Dominance, Misuse of the Regulatory Process and Product Hopping

The EU Pharmaceutical Inquiry concluded that that originator companies sometimes misuse the regulatory process to delay or block the entry of competitors. In 2012, the European Court of Justice upheld the 2010 decision of the EU General Court which upheld the EC's finding of 2005, that AstraZeneca abused its dominant position to hinder generic competition for its anti-ulcer medication Losec. This Court of Justice ruling clarified several issues related to market definition, dominance and abuse as specified in Article 102 TFEU. The first abuse involved the provision of misleading information to national patent offices with the aim of delaying or preventing the market entry of generics. The second abuse involved the deregistration of the market authorization of Losec capsules in certain countries, with the aim of raising barriers against generic entry and parallel trade (because at the time generics could only be marketed and parallel importers could only obtain a licence if there was a market authorization for a reference product.). The Court stated that a firm which holds a dominant position has a special responsibility under Article 102 and that it cannot therefore use regulatory procedures in

¹²⁴ "Antitrust: Commission Fines Lundbeck and Other Pharma Companies for Delaying Market Entry of Generic Medicines." June 19, 2013. http://europa.eu/rapid/press-release_IP-13-563_en.htm

¹²⁵ Bruce, F. "'Appalled' Lundbeck appeals pay-for-delay fine." Scrip Intelligence. September 2, 2013. <http://www.scripintelligence.com/policyregulation/Appalled-Lundbeck-appeals-pay-for-delay-fine-346171>

¹²⁶ Bruce, F. "'Appalled' Lundbeck appeals pay-for-delay fine." Scrip Intelligence. September 2, 2013. <http://www.scripintelligence.com/policyregulation/Appalled-Lundbeck-appeals-pay-for-delay-fine-346171>

such a way as to make more difficult the entry of competitors, in the absence of objective justification.¹²⁷

Commentary

This case raises similar issues related to life cycle management strategies as the product hopping cases in the US. In the EU these are being addressed as abuse of a dominant position in use of regulatory proceedings, which requires a showing of dominance. In the US the complaints are based on a more general Sherman Section 2 concern for monopolization, for which the originator's monopoly on the molecule is assumed. Thus in the US these actions appear to be less restricted to originator firms that have a dominant position within their therapeutic class.

4. Mergers and Acquisitions

Similar to the US, the EU requires prenotification of mergers and joint ventures, and approval may require divestiture of assets in classes where the merger increases concentration. The EU examines increase in potential market power within a market, which has both product and geographic dimensions. The product dimension is defined by substitutability in demand. Geographic markets are defined at the country level because market access registration is by member state.

To illustrate product market definition: In the Astra Zeneca case, the Commission cited the fact that the proton pump class of anti-ulcerants had grown steadily, at the expense of the H2-antagonists, to conclude that the H2-antagonists are not part of the same class as the proton-pump inhibitors. Of note is that the discussion attributed these divergent trends to therapeutic superiority of the proton-pump inhibitors, and did not consider the role of manufacturer promotion, which probably focused on the newer, proton-pump inhibitor class as patents expired on the older H2-antagonists. In reality, both product superiority and differences in patent life and promotion probably played a role.

VI. Conclusions and Implications for Middle and Lower Income Countries (MLICs)

This review of antitrust and competition policy towards the pharmaceutical industry in the US and EU suggests that basic principles are similar across countries. However, important differences exist, arising partly out of differences in the patent regimes, regulatory policies, health insurance and other institutional factors that shape the competitive environment of the pharmaceutical industry in each country. This section summarizes the main findings from the experience in the US and EU and discusses implications for antitrust and competition policy in MLICs, including similarities and differences.

1. Mergers and Acquisitions (M&A)

Pharmaceutical products The biopharmaceutical industry has experienced extensive M&A activity in recent years, involving both originator and generic firms. These mergers often span multiple countries, because firms in this industry are increasingly global, with focus on growth in emerging markets. MLICs have therefore experienced consolidation of the local businesses of multinational firms; targeted acquisitions of local firms by multinationals (e.g. Sanofi's acquisition of Medley in Brazil); and consolidation of local firms. Prenotification of mergers to competition authorities in each affected country should be the norm, because geographic markets for drugs are national, reflecting market access regulation by national authorities. Prenotification enables each national authority to evaluate the effects of the merger on concentration in its markets, requiring divestiture of overlapping products if

¹²⁷ "Antitrust: Commission welcomes Court of Justice judgment in the Astra Zeneca case. European Commission. December 6, 2012. http://europa.eu/rapid/press-release_MEMO-12-956_en.htm

necessary to prevent competitively harmful increases in concentration. How M&A prenotification value thresholds should be scaled in proportion to a country's GDP or pharmaceutical sales is an important policy issue. Prenotification entails costs, delay and uncertainty for the merging firms, hence setting very low value thresholds could discourage beneficial entry or consolidation. It is noteworthy that the US has extended its prenotification requirements to licensing deals, reflecting the importance of licensing deals as a form of acquisition in the pharmaceutical industry.

In evaluating mergers, antitrust authorities consider the competitive impact in each therapeutic class represented by the merging firms' product portfolios. Geographic markets are at the national level. Product markets for on-patent drugs are defined by therapeutic class or indication, to include all compounds that physicians consider therapeutic substitutes. For off-patent drugs, the product market is usually defined by the molecule, because generics are extremely close substitutes. For both originators and generics, market participants may include products in late stage clinical trials that are close to market entry. Mergers are frequently approved conditional on divestiture of overlapping products and/or classes of products, preferably to competitors or potential entrants.

Predicting potential anticompetitive effects of a merger of pharmaceutical companies entails estimating potential coordinated and unilateral effects using standard measures, including the HHI index and other measures of concentration and the diversion ratio for predicting unilateral effects of a merger involving differentiated products, which is typical for on-patent drugs. In applying any measure involving cross-elasticity to the pharmaceutical industry, it is important to recognize that insurance coverage makes patient demand highly price-inelastic, for both cross-price and own-price elasticities. This price-insensitivity usually extends to physicians who prescribe drugs as patient agents and are often uninformed about drug prices, unless the physicians themselves are financially at risk for drug costs as part of the patient's insurance coverage. Thus analysis of potential competitive harms from mergers should consider all aspects of cross-elasticity, not simply price effects, especially when patients are insured. In general, a finding of low cross-price elasticity between two drugs does not necessarily imply that they are in different markets.¹²⁸

Retail Pharmacy Mergers Acquisitions to consolidate retail pharmacies into regional or national chains are common, to capture economies of scale that can potentially benefit consumers. However, antitrust should monitor and block mergers that pose a threat to competition in pharmacy markets measured at the local level. The US FTC has permitted pharmacy consolidation but monitors the effects of proposed mergers on concentration at the local pharmacy market level. The FTC has blocked some regional consolidations or required divestitures to preempt concentration in local pharmacy markets.

To further promote competition in retail pharmacy, the US permits entry of pharmacies located in supermarkets and mass merchandisers like Walmart, provided that these pharmacies hire licensed pharmacists to dispense prescription drugs. OTC products are available to consumers in supermarkets in the US even without a licensed pharmacist. These rules permit retail pharmacies to realize economies of scale from chain formation, while preserving competition in local markets and wide access to prescription and OTC drugs for consumers. EU countries are slowing following the US in relaxing their rules against chain pharmacies, against pharmacies based in supermarkets and against sale of OTC products outside pharmacies. The evidence from the US and EU suggests that such constraints on competition are harmful to competition and consumer choice, and are not necessary to protect consumer safety.

¹²⁸ See Statement of Commissioner Rosch in FTC vs. Lundbeck Inc. Jan. 20 2012.

2. Agreements Not to Compete

Agreements on price Collusion on prices of pharmaceuticals could in theory occur among drug manufacturers that set ex-manufacturer prices and/or among retail pharmacies that set retail prices to consumers. In practice, allegations of collusion on price for on-patent prescription drugs have been rare in the US and EU, despite the oligopolistic market structure of most on-patent therapeutic classes. This may reflect several factors, including: originator products are differentiated; originator firms face different competitors in each therapeutic class; drug prices are regulated in most countries ex- US, which preempts price increases; although drug prices are not regulated in the US, demand is highly inelastic due to patents and insurance, which enables high prices without collusion; and discounting in the US to individual payers is confidential to help undermine any propensity for collusion. Cartels have occurred among manufacturers of OTC products, notably vitamins, which are less differentiated, have more price-elastic firm-specific demand because they are not covered by insurance, and lack the countervailing power over prices of powerful payers.

Horizontal price agreements on retail prices charged by pharmacies are preempted in most EU countries through regulation of pharmacy margins and retail drug prices, which are enforced through insurance reimbursements. Similarly, in the US, public and private payers negotiate pharmacy margins and co-payments charged to patients by pharmacies, and these price limits are enforced through payer reimbursement to pharmacies. Allegations that pharmacies have colluded in setting their dispensing fees to payers have occasionally occurred. Antitrust authorities have permitted such collective pharmacy fee setting only if it is necessary as part of a risk-sharing arrangement between the pharmacies.¹²⁹

In MLICs, the absence of powerful payers that regulate or negotiate drug prices with manufacturers and pharmacies as part of their drug reimbursement processes may imply a greater need in MLICs for antitrust authorities to monitor for horizontal agreements on price by drug manufacturers or retail pharmacies. The recent price fixing case by retail pharmacies in Chile illustrates the dangers of anticompetitive drug pricing when pharmacies are consolidated into chains.

The potential for anticompetitive agreements on drug prices in MLICs also arises in the context of drug procurement by public hospitals and clinics, that often conduct competitive tenders to select reimbursed drugs. Such tendering can be pro-competitive, by encouraging price competition between substitutable drugs to achieve preferred formulary status. However, tendering processes may also be manipulated by manufacturers for price-fixing and/or market sharing agreements, sometimes implemented through wholesalers. Anti-trust monitoring of these procurement processes of public hospitals and clinics is important to assure that they are pro-competitive, rather than mechanisms to implement collusive pricing or market sharing.

Pay-for-delay agreements and barriers to generic competition Pay-for-delay agreements, whereby originator firms pay generics to delay entry, have been a major focus of antitrust actions in the US and the EU. Such agreements can prolong the period of originator monopoly rents which can be shared among the parties to the agreement. They usually arise out of the generic's challenge to the originator patents, in order to enter prior to expiry of all patents, and the originator's counterclaims of patent infringement. This litigation is typically settled with an agreement for generic entry at some intermediate date between the generic's regulatory approval date and the latest patent expiration date.

¹²⁹ Pharmacies in some states have lobbied for "any willing provider" laws that require payers to deal with any pharmacy that accepts their terms. Such laws are a legal restraint on competition through selective contracting.

Patent litigation settlements must be reported to anti-trust authorities in the US and the EU, and are accepted without challenge if they simply agree to a date of generic entry. However, such agreements are challenged in both the US and EU when they include payment in some form by the originator to the generic company. Such payment raises the possibility that the agreed generic entry date extends the monopoly rents which are then shared through the payment from the originator to the generic. The US Supreme Court recently ruled that such agreements with payment should be subject to a rule of reason analysis, even if the agreement provides for generic entry within the scope of the patent term. The Court rejected the FTC's position, that agreements with payment should also shift the burden of proof to the defendants.¹³⁰ Note that such anticompetitive agreements can occur despite the potential for entry by other generics because other entrants would incur time and resource costs of challenging patents; moreover, they would face competition from the agreeing generics and therefore have lower expected profits, because the pay-for-delay agreements often provide for termination of the payments if other generics enter.

In MLICs, pay-for-delay agreements may so far be uncommon for several reasons. First, because most MLICs do not require that all generics meet bioequivalence requirements, quality of generic products is uncertain and generics therefore compete on brand as a proxy for quality, not on price. In such branded generic markets, originators maintain high prices and significant market shares even after generic entry, hence originators have less incentive to pay generics to delay entry. Second, those MLICs that do not recognize secondary patents on existing, patented molecules may see fewer patent challenges and hence less opportunity for pay-for-delay settlements to such challenges, than countries like the US that do permit follow-on patents. These follow-on patents are more likely to be successfully challenged than are the original, composition-of-matter patents. Generics in the US therefore often challenges the secondary patents and originators may be more willing to settle such cases.

Although generic markets in MLICs may be less prone to pay-for-delay settlements, anti-trust authorities should require the reporting of settlements between originator and generic companies arising out of patent litigation and possibly other contexts, in order to monitor pay-for-delay and any other potentially noncompetitive agreements. In particular, "payment" may be suspect if it is excessive for services received or for services that are unnecessary or highly unusual. For example, an agreement whereby an originator pays a generic firm to co-promote its products may be suspect if it arises out of litigation late in the product life-cycle, whereas a similar agreement at originator launch could be a legitimate effort to increase sales of the new product.

Anti-trust authorities in MLICs may also need to monitor other barriers to generic entry that do not arise in high income countries because of the role of insurers or other factors. In particular, pharmacies in the US are incentivized by payer reimbursement rules to substitute generics for originator drugs whenever possible and to seek out cheaper generics. US payers also incentivize patients to accept generics by raising patient co-payments on off-patent originator drugs once generics are available. Generic penetration thus rapidly rises to 80- 90% of originator sales within 6-12 months of generic entry in the US. By contrast, pharmacies in MLICs often earn higher margins on higher-priced originator drugs than on generics. Originator manufacturers may encourage pharmacies not to substitute generics through discounts on originator drugs and in MLICs there is no powerful payer to squeeze pharmacy margins by controlling the retail prices charged by pharmacies. In such contexts, antitrust authorities can play an important role in promoting generic competition, by advocating for and monitoring regulations that require pharmacies to stock generics from competitor companies, not just their store brand, and inform patients of generic availability. These pro-generic policies could reinforce structural

¹³⁰ FTC v. Actavis, No. 12-416, 570 U.S. ___ (June 17, 2013).

policies to encourage competition in retail pharmacy markets, including antitrust blocking of mergers that permit local market power, and regulatory policies to permit supermarkets and other mass merchandizers to have in-store pharmacies, operated by licensed pharmacists, to provide a competitive check on the market power of retail pharmacy chains.

There is also a concern in some MLICs that heavy brand advertising of branded generics can undermine competition by increasing costs of entry. However, since brand advertising can also be informative about product quality when quality is not assured by regulation, competition policy would need to weigh any information benefits from brand advertising against any harm to competition, which would be both theoretically and empirically challenging. Using regulatory policy to eliminate quality uncertainty through a bioequivalence requirement is likely the preferable policy approach. Given a bioequivalence requirement that eliminates meaningful quality differences, any information value in brand advertising is eliminated. Competition policy might then presume that such advertising is harmful to competition and to consumers.

3. Other Monopolization Issues

Pharmaceuticals are intentionally subject to significant entry barriers. Patents are necessary to incentivize innovation, and regulatory requirements for evidence of safety and efficacy prior to market access are important to protect patient safety and avoid wasteful expenditures. However, these legitimate entry barriers may be abused, and antitrust can play an important role in preventing such abuse.

Patent “evergreening” Antitrust authorities in both the US and the EU have challenged “patent evergreening” , that is, the filing by originator firms of follow-on patents that may have little merit and are unlikely to withstand legal challenge. Such patents nevertheless raise costs for generics that must successfully challenge every filed patent before they can come to market. Frivolous patenting raises health care costs for consumers and reduces timely patent reviews by patent offices, which have limited resources. In the US, state Attorneys General have successfully filed frivolous patenting actions and won significant fines, arguing that delayed generic entry has raised costs for state health care programs. The EU has also argued that filing by originator firms of excessive “patent thickets” may raise costs and deter entry of other innovator firms that must obtain licenses. Originator incentives for patent evergreening are probably weaker in most MLICs, because originators generally maintain high prices and shares after generic entry. Nevertheless, competition authorities should be aware of the potential for such practices.

Product hopping “Product hopping” occurs when an originator firm launches minor product reformulations that offer little or no therapeutic benefit, but effectively block generic competition simply because they are different. This is usually done prior to patent expiry and generic entry on the original formulation. The originator firm persuades physicians and patients to switch to the new formulation by raising the price of the original product above the new formulation, switching all marketing efforts to the new formulation and sometimes removing the original formulation from the market. Because, under U.S. and EU substitution laws, pharmacies may only substitute generic products of exactly the same formulation as the patent-expired originator formulation, shifting prescriptions to the new formulation effectively blocks pharmacy substitution and generic competition.

Prosecuting such cases under anti-trust law is relatively recent in the US and the EU. The US FTC has not itself filed such actions directly but it has written in support of a private action. Because product changes are often procompetitive, product hopping claims must show that the competitive harm from blocking generics outweighed any competitive gain from new product availability.

Product hopping cases may arise less in MLICs, because pharmacies may *de facto* substitute between broadly similar products, not just between interchangeable generics of the identical formulation as the originator, and originators retain large market shares after generic entry. In such contexts, originators have less incentive to engage in reformulation to block generic substitution, in order to maintain their sales. Moreover, branded generics in MLICs rely more on their own promotion to grow sales, not relying simply on pharmacy incentives for generic substitution as in the US. Nevertheless, as more MLICs move to regulating market access of generics and interchangeability based on the generic showing bioequivalence to the reference originator product, it becomes important to monitor any anticompetitive withdrawal of the originator product to either block generic approval or generic substitution.

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