Pharmaceutical Industry Antitrust Handbook

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CHAPTER I

MARKET PARTICIPANTS AND COMPETITION

A. Market Participants

Pharmaceuticals[1] play a major role in the U.S. economy and in the health of Americans. Billions of prescriptions are filled annually, costing well over a hundred billion dollars. For example, in calendar year 2007, retail outlet sales of prescription drugs totaled $227.5 billion.[2] And between October 2004 and September 2005, 3.6 billion prescriptions were filled in this country.[3]

Expenditures on pharmaceuticals are growing and represent an increasing percentage of health care expenditures. In the ten years from 1990 to 2000, "annual spending on prescription drugs in the United States grew nearly twice as fast as total national health expenditures."[4] Spending for prescription drugs has continued to increase in the years since 2000. For instance, spending increased 30.7 percent in 2000-2002, 10.5 percent in 2003, 8.4 percent in 2004, 5.8 percent in 2005, 8.6 percent in 2006, and 4.9 percent in 2007.[5] In 2007, prescription drugs accounted for 10 percent of aggregate health spending and this number is expected to increase to 12 percent by 2016.[6]

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1. Pharmaceuticals includes both conventional drugs and biological drugs.
2. *See* CTRS. FOR MEDICARE & MEDICAID SERVS. (CMS), NHE WEB TABLES, NATIONAL HEALTH EXPENDITURE DATA AGGREGATE AMOUNTS AND AVERAGE ANNUAL PERCENT CHANGE, BY TYPE OF EXPENDITURE: SELECTED CALENDAR YEARS 1960-2007, Tbl. 2 [hereinafter CMS, NHE WEB TABLES], http://www.cms.hhs.gov/NationalHealthExpendData/downloads/tables.pdf.
3. *See* PHARM. RESEARCH & MFRS. OF AM. (PHRMA), PHARMACEUTICAL INDUSTRY PROFILE 2006 52 (2006), *available at* http://www.phrma.org/files/2006%20Industry% 20Profile.pdf.
4. *See* CONG. BUDGET OFFICE (CBO), ISSUES IN DESIGNING A PRESCRIPTION DRUG BENEFIT FOR MEDICARE 1 (2006) [hereinafter CBO, ISSUES IN DESIGNING], *available at* http://www.cbo.gov/ftpdoc.cfm?index=3960&type=0&sequence=0.
5. *See* CMS, NHE WEB TABLES, *supra* note 2, at Tbl. 2.
6. *See id.*; Express Scripts Inc., Annual Report (Form 10-K), at 1 (Feb. 21, 2008).

Part of the increase in spending is attributable to new and more expensive drug treatments, and part is attributable to use of prescription pharmaceuticals by more people. New drugs are generally more expensive than older drugs but may be more effective and produce fewer adverse side effects. Patients have become more aware of new drugs because of pharmaceutical manufacturers' advertising directly to consumers and are asking their physicians to prescribe advertised pharmaceuticals. People of all ages who reported using at least one prescription drug during the past month rose from 39 percent during 1988-94 to 45 percent during 1999-2002.[7] For people 65 years and older, the increase in drug use was even greater, from about 74 percent to 85 percent over the same period.[8] Part of the increase in spending is attributable to the Medicare Part D prescription benefit.[9]

With pharmaceuticals representing such an important part of the nation's economy and the health care sector, competition in the pharmaceutical industry is crucial to provide the best quality drugs for the lowest possible price. Antitrust enforcement plays a key role in ensuring competition in this industry.

1. Branded Manufacturers

Branded pharmaceuticals (here, referred to as "branded" or "brand") are sold under a trade name. Generally, they are innovative drugs (comprising either chemistry-based or biologic pharmaceuticals) that enjoy or enjoyed protection by one or more patents. They are also referred to as innovator or pioneer drugs.

7. NAT'L CTR. FOR HEALTH STATISTICS, HEALTH, UNITED STATES 2006, Tbl. 93 (2006), http://www.cdc.gov/nchs/data/hus/hus06.pdf.
8. *Id.*
9. *See* Press Release, IMS, IMS Reports United States Prescription Sales Jump 8.3 Percent in 2006, to $274.9 Billion (Mar. 8, 2007), *available at* http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_80415465,00.html.

a. Drug Discovery Process

Pharmaceutical companies spend an average of ten to 15 years researching a new drug.[10] For every 5,000 to 10,000 compounds tested, 250 undergo preclinical testing.[11] Of these, five will go into clinical trials, and only one ultimately will receive approval from the United States Food and Drug Administration (FDA).[12] A discussion of the regulatory aspects of the drug discovery process are set forth at Chapter II.A.

b. Large Research and Development Costs

An industry trade association, Pharmaceutical Research and Manufacturers of America (PhRMA), estimates that the cost of developing one new medicine is approximately $1.3 billion.[13] According to PhRMA, in 2007, the pharmaceutical industry expended an estimated $58.8 billion on research and development.[14]

c. Patent Protection

In the United States, patents give the inventor exclusive rights to sell an invention for 20 years. The exclusivity provided by our patent system fosters innovation, which benefits consumers.

Many brand drugs enjoy patent protection when they are introduced to the market. However, patents often are granted before FDA approval; therefore, several years of patent protection may expire before the

10. *See* PHARM. RESEARCH & MFRS. OF AM. (PHRMA), PHARMACEUTICAL INDUSTRY PROFILE 2008 3 (2008) [hereinafter PHRMA 2008 INDUSTRY PROFILE] (citations omitted), *available at* http://www.phrma.org/files/2008%20Profile.pdf.
11. *Id.*
12. *Id.* at 4.
13. *Id.* at 2.
14. *Id.* at 2, 3.

manufacturer is permitted to market the drug.[15] Generally, once all patents protecting a drug have expired, generics enter the market.

d. Competition with Other Drugs in Therapeutic Category

Even though a patent may protect a drug from competition with a generic, the patented drug may be one of several drugs that physicians can prescribe to treat a particular disease. Thus, a manufacturer of a patented drug may compete with other manufacturers' branded drugs to persuade physicians to prescribe its product. The manufacturer of a patented drug may also have to compete to be included in a pharmacy benefit manager's (PBMs) formulary of drugs that are covered under a health insurance plan (discussed further below at Section 4(d)(3)).[16]

e. Biotech and Biologics

In recent years, the development of pharmaceuticals has expanded from chemistry to biotechnology. "Biotechnology" is "a collection of technologies that capitalize on the attributes of cells, such as their manufacturing capabilities, and put biological molecules, such as DNA and proteins," to work for patients through the creation of "biologic" drugs.[17]

Most biologics are complex mixtures that are not easily identified or characterized. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources—human, animal, or microorganism—and may be produced by biotechnology methods and other cutting-edge technologies.

15. *See* FED. TRADE COMM'N (FTC), GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 4 (2002) [hereinafter FTC, GENERIC DRUG ENTRY], *available at* http://www.ftc.gov/os/2002/07/genericdrug study.pdf.
16. *See* CBO, ISSUES IN DESIGNING, *supra* note 4, at 14; FTC, GENERIC DRUG ENTRY, *supra* note 15, at 7.
17. Biotechnology Industry Organization (Bio), Biotechnology: A Collection of Industries (May 4, 2009), http://www.bio.org/speeches/pubs/er/technology_collection.asp.

Gene-based and cellular biologics, for example, often are at the forefront of biomedical research.

The biotechnology industry has grown significantly since the early 1990s. For instance, U.S. health care biotech revenues increased from $8 billion in 1992 to $58.8 billion in 2006.[18] As of August 2007, over 300 biotech drugs had been approved by the FDA and two thousand were in development.[19]

Biotechnology is very research-intensive and costly. In the U.S., publicly-traded biotechnology companies spent over $27 billion on research and development in 2006 alone.[20]

Various relationships are developing between the traditional chemistry-based pharmaceutical companies and biologic companies. As chemistry companies struggle to fill their pipelines, they have looked to biologics for new drugs to market. Chemistry-based and biotechnology companies have joined in various arrangements: acquisitions, mergers, licensing agreements, and joint ventures.

2. Generic Manufacturers

a. Generic Drugs

A generic drug is required to contain the same active ingredient as a pharmaceutical previously approved by the FDA; be identical in strength, concentration, dosage form, and route of administration; have the same

18. Biotechnology Industry Organization (Bio), Biotechnology Industry Facts (May 4, 2009) [hereinafter Bio, Biotechnology Facts], http://www.bio.org/speeches/pubs/er/statistics.asp.
19. *See* PHARM. RESEARCH & MFRS. OF AM. (PhRMA), 2007 ANNUAL REPORT 4 (2007), *available at* http://www.phrma.org/files/2007%20Annual%20Report.pdf.
20. *See* Bio, Biotechnology Facts, *supra* note 18.

indications; and be bioequivalent[21] to the brand pharmaceutical.[22] The overall development process for generic drugs is significantly shorter than for brand drugs, but the FDA approval process for generic drugs may be longer than for brand drugs. (The FDA approval process is addressed in Chapter II.)

According to the Generic Pharmaceutical Association (GPhA), generic medicines account for 69 percent[23] of all prescriptions dispensed in the United States, but they account for only 16 percent of all dollars spent on prescriptions.[24] Generic drug manufacturers frequently sell their product at substantial discounts from their brand name competitors, reflecting the lower cost of development and competitive pressures.

A pharmacist is permitted to substitute a generic for the corresponding brand drug unless the physician has prescribed the brand and stipulated that the prescription must be dispensed as written. In fact, many state laws require generic substitution. Generic pharmaceutical products are used to fill nearly 2.6 billion prescriptions every year.[25]

There are generic copies of both prescription and over-the-counter (OTC) medicines. As of yet, there is no FDA approval process for

21. The FDA has generally defined the term "bioequivalent" to mean "the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study." 21 CFR § 320.1(e). The regulation also provides additional instruction as to when bioequivalence may be determined when there is a difference in the rate of absorption. *See id.*
22. *See* Generic Pharm. Ass'n (GPhA), About Generics, FAQs, http://www.gphaonline.org/Content/NavigationMenu/AboutGenerics/FAQs/default.htm.
23. Generic Pharm. Ass'n (GPhA), Facts at a Glance [hereinafter GPhA Facts], http://www.gphaonline.org/about-gpha/about-generics/facts. The FTC reported in 2002 that 47 percent of prescriptions were generics compared to 19 percent in 1984. FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY (2002), *available at* http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf.
24. *See* GPhA Facts, *supra* note 23.
25. *See id.*

generic biologics, although generic manufacturers have been pushing FDA to devise an approval process for generic biologics and legislative proposals have been offered in Congress.

b. Generics Compete Based on Price

Generics compete with brand drugs and other generics largely based on price. According to an FDA assessment, the first generic to enter the market is priced at around 94 percent of the price of the brand.[26] The entry of a second generic, however, impacts price more significantly, reducing the price of the generics to just over half (around 52 percent) of the brand drug's price.[27] As additional generics enter the market, the price of the generics continues to fall at least until the fifth entry.[28] With multiple generics, the price drops to as much as 80 percent below brand price.[29] In 2007, the average price of a generic prescription drug was $34.34.[30] The average price of a brand name prescription drug was $119.51.[31] Profit margins on generics become very thin once multiple generics are available.

26. Food & Drug Admin. (FDA), Generic Competition and Drug Prices (Apr. 4, 2006), *at* http://www.fda.gov/cder/ogd/generic_competition.htm [hereinafter FDA, Generic Competition] (analyzing generic drug competition utilizing IMS retail sales data for single-ingredient brand name and generic drug products sold in the United States from 1999-2004).
27. *Id.*
28. *See* David Reiffen & Michael R. Ward, *Generic Drug Industry Dynamics* (FTC Bureau of Econ., Working Paper No. 248, 2002), *available at* http://www.ftc.gov/be/econwork.htm; *see also* FDA, Generic Competition, *supra* note 26 (noting that "[a]s additional generic manufacturers market the product, the prices continue to fall, but more slowly. For products that attract a large number of generic manufacturers, the average generic price falls to 20% of the branded price and lower").
29. Generic Pharm. Ass'n (GPhA), The Case for Generics [hereinafter GPhA, Case for Generics), http://www.gphaonline.org/about-gpha/about-generics/case.
30. GPhA Facts, *supra* note 23.
31. *Id.*

c. Relative Importance of Brand and Generic Pharmaceuticals

Generics' share of prescription volume has grown over the last 20 years and currently is between 50 percent and 70 percent. In 1984, it was 19 percent and, in 2007, it had reached 67 percent.[32] In 2006, the ratio of generic to brand by volume (weighted average) was 58:42.[33]

Generics' share of dollar sales is much lower. While generics accounted for 69 percent of all prescriptions dispensed in 2007, according to IMS Health data, they accounted for only 16 percent of all dollars spent on prescription drugs.[34] In terms of dollar sales, U.S. brand pharmaceutical sales for 2007 were $228 billion, whereas U.S. generic pharmaceutical sales were only $58.5 billion.[35]

d. Brand and Generic Manufacturing Companies

No bright line exists between brand and generic manufacturing companies. On one hand, brand manufacturers have generic divisions. One example is Novartis AG with its Sandoz division, which manufactures and markets generics. On the other hand, generic companies have tried to improve their margins by developing innovative drugs. Teva Pharmaceutical Industries Ltd. is known as a large generic manufacturer that also develops innovative drugs. Based on the number of prescriptions dispensed, the top five generic companies are Teva, Mylan, Inc., Novartis (Sandoz), Watson Pharmaceuticals, Inc. and

32. *See* IMS Health, National Prescription Audit Plus 2001 (1984-2000 data); Press Release, IMS Health, IMS Health Reports U.S. Prescription Sales Grew 3.8 Percent in 2007, to $286.5 Billion (Mar. 12, 2008), *available at* http://imshealth.com/portal/site/imshealth/menuitem.a46c6d4df3db4b3d88f611019418c22a/?vgnextoid=280c1d3be7a29110VgnVCM10000071812ca2RCRD&vgnextfmt=default.
33. PHARM. RESEARCH & MFRS. OF AM. (PHRMA), PHARMACEUTICAL INDUSTRY PROFILE 2007, Key Facts (2007), *available at* http://www.phrma.org/files/Profile%202007.pdf.
34. GPhA Facts, *supra* note 23.
35. *Id.* (referring to IMS Health as source of data).

Mallinkrodt, respectively.[36] Several of these top generic manufacturers also make branded products.[37]

e. Manufacturer Consolidation

There has been considerable consolidation among pharmaceutical manufacturers. Some examples are: Pfizer Inc. acquired Pharmacia Corporation and Warner-Lambert Company; Hoechst AG and Rhone-Poulenc, S.A. merged to form Aventis, S.A.; Novartis A.G. emerged from the merger of CIBA-Geigy Corporation and Sandoz Corporation; Teva acquired Ivax Corporation; Watson Pharmaceuticals, Inc. and Schein Pharmaceuticals, Inc. merged and later Watson acquired Andrx Corporation; Barr Pharmaceuticals acquired Pliva d.d.; Teva subsequently acquired Barr, and these are only a few examples. Many factors motivate mergers, including a need to fill a company's pipeline of promising drugs in development or to increase the research and development capability, a desire to enter new geographic markets, an opportunity to acquire a company with a drug in an area where the acquirer has a strong marketing force, and many others. Mergers and acquisitions among manufacturers will be discussed in detail in Chapter IV.

3. Drug Wholesalers

a. Distribution Function

Wholesalers distribute brand, generic, and specialty drugs.[38] They deliver drugs to retail pharmacies, mail pharmacies, mass merchandisers, food stores, hospitals, long-term care facilities, home health facilities, clinics, and physicians' offices. Wholesalers even serve pharmacy chains that operate their own warehouses because, typically, chain warehouses stock large volume items, whereas drug wholesalers provide

36. *Id.*
37. *Id.*
38. *See* Health Care Distrib. Mgmt. Ass'n (HDMA), Role of Distributors (2009) [hereinafter HDMA, Role of Distributors], http://www.healthcaredistribution.org/education/learn.asp.

the smaller volume items to the chains' stores. Wholesalers deliver specialty drugs to physicians' offices, patients' homes, and retail pharmacies.

Manufacturers may offer drugs at discounted prices, which are purchased by so-called secondary wholesalers.[39] Pharmaceutical companies offer discounted prices at various points during the year for a variety of reasons (e.g., to meet quarterly sales goals or to clear product inventory in advance of price increases).[40] To take advantage of the discounted price and recoup their capital investment, secondary wholesalers must resell the discounted drugs quickly to wholesalers.[41] This discounted drug distribution may involve several transactions among wholesalers before the drugs are finally sold to the dispensing entity.[42]

Wholesalers typically deliver products within 24 hours of the customer placing an order, and in even shorter intervals for hospitals. To achieve such rapid delivery, national wholesalers must operate distribution facilities around the country.

Pharmacy customers expect wholesalers to be able to fill 99 percent of their orders when submitted.[43] Therefore, wholesalers must maintain a sufficiently broad inventory to be able to achieve that fill rate. Wholesalers' warehouses generally maintain more than ten thousand products in inventory.[44] Other functions performed by wholesalers include extending credit and providing receivables management to their customers.[45]

Wholesalers operate on thin margins. As a result, they have sought innovations to automate product selection within their warehouses and to control inventory. In addition, wholesalers have introduced electronic

39. *See* FOOD & DRUG ADMIN. (FDA), PROFILE OF THE PRESCRIPTION DRUG WHOLESALING INDUSTRY, FINAL REPORT § 1.5.4 (2001) [hereinafter FDA FINAL REPORT], *available at* http://www.fda.gov/oc/pdma/report2001/attachmentg/toc.html.
40. *See id.* § 1.3.4.
41. *See id.* § 1.5.4.
42. *See id.*
43. *See* HDMA Role of Distributors, *supra* note 38.
44. *See id.*
45. *See id.*

order entry systems to make ordering more efficient. These electronic systems also allow retailers to check the wholesaler's inventory for product availability. The earlier electronic ordering systems were software-based, but wholesalers have introduced Web-based ordering systems that making pharmacies download software.

Distribution through an intermediary wholesaler can promote economic efficiencies and reduce costs by minimizing the number of transactions required to distribute drug products from manufacturer to patient.[46] For example, wholesale distributors may reduce the number of small volume sales for drug manufacturers and relieve health care providers and retailers from the burden of dealing with several separate manufacturers.[47]

In the past, drug manufacturers have used inflation-based models to compensate wholesalers for their distribution services.[48] Under this system, a wholesaler may purchase and hold pharmaceutical inventory in advance of manufacturer price increases, allowing the wholesaler to benefit from a higher profit margin. Manufacturers, however, have sought to increase control over the amount of drug product available in the supply chain in order to stabilize demand and inventory requirements, and to reduce the risks associated with a large amount of product in the secondary market (e.g., counterfeiting, drug diversion, product expiration). Consequently, the use of inflation-based compensation for wholesalers has gradually been phased out in favor of a fee-for-service compensation model.

b. Higher Margin Services

Wholesalers have moved into functions (beyond distribution) that command higher margins, such as automation technology for hospitals. Wholesalers provide, among other services, centralized pharmacy

46. *See* HEALTH CARE DISTRIB. MGMT. ASS'N, 2003 HDMA INDUSTRY PROFILE AND HEALTH CARE FACTBOOK (2003) [hereinafter 2003 HDMA INDUS. PROFILE].
47. *See* FDA FINAL REPORT, *supra* note 39, § 1.2.
48. *See, e.g.*, AmerisourceBergen Co., Annual Report (Form 10-K), at 6 (Dec. 9, 2005); McKesson Corp., Annual Report (Form 10-K), at 9; Cardinal Health, Annual Report (Form 10-K), at 7 (June 30, 2006).

automation systems for unit-dose medications, unit-based cabinet technologies to store drugs securely and permit rapid retrieval, point-of-use supply automation systems for inventory management, and automated drug administration systems to ensure accuracy at the point of treatment. These systems are intended to reduce hospitals' costs and possibility of error.

c. Additional Services for Retail Pharmacies

Wholesalers manufacture and market automated dispensing systems for retail pharmacies as well as for hospitals. Wholesalers also provide software and consulting services to pharmacies. As examples, wholesalers provide supply management software, workflow management software, inventory management services, reimbursement services, software for Internet claims adjudication, physician education programs, and logistics services. Wholesalers also provide clinical support and treatment compliance programs, and furnish software for disease state management. In addition, wholesalers offer automated prescription package labeling programs to reduce labor costs in a healthcare institution's pharmacy department.

d. Services Targeted to Independent Pharmacies

Wholesalers provide additional services to independent retail pharmacies to help them compete with pharmacy chains. Wholesalers operate cooperative advertising programs, franchise programs, merchandising programs, store display service programs, customer loyalty programs, and group buying programs. Wholesalers offer programs that automatically ship new prescription drugs to pharmacies so that they will have the latest drugs in their inventory. To assist independent pharmacies with their cost of drugs, wholesalers negotiate prices with generic manufacturers and provide private label products.[49]

Wholesalers offer programs related to a pharmacy's business beyond pharmaceuticals, such as ATM machine programs, contact lens

49. *See, e.g.*, Pharmacy First, Wholesale Alliance LLC, http://www.pharmacyfirst.com/pf_wholesalealliance.asp.

programs, photo processing services, and greeting card programs. Wholesalers help pharmacists fulfill continuing education requirements by organizing continuing education sessions.

A single independent pharmacy could not perform these functions at as low a cost on its own as wholesalers can for their many independent pharmacy customers.

e. Repackaging

Some wholesalers engage in repackaging of pharmaceuticals. They purchase bulk containers of pills from manufacturers, which may contain thousands of pills and are less expensive than smaller packages. The repackaging facility then places the pills in smaller containers that correspond more closely to prescription size. The smaller packages often provide convenience, particularly to hospitals and nursing home facilities.

f. Consolidation

Drug wholesaling has undergone considerable consolidation. For one thing, wholesalers consolidate through contract by forming alliances to leverage their buying power. For another, many local and regional wholesalers have been acquired or gone out of business. Even national wholesalers have merged.

Local and regional wholesalers continue to compete among themselves and with national wholesalers. These wholesalers compete by concentrating on a particular geographic area. There are also wholesalers that serve niche markets such as specialty pharmaceuticals.

4. Pharmacy Benefit Managers

a. Origins of PBMs

PBMs began as agents to adjudicate prescriptions electronically to assist health plans, pharmacies and patients, a function they still perform. A patient presents a prescription and an insurance card to a pharmacist. The pharmacy's computer is connected to the PBMs computer, which allows the pharmacist to verify that the patient has prescription coverage

for the particular drug and determine the amount of copayment to collect from the patient. The pharmacist then fills the prescription and collects the copayment. The PBMs computer logs the amount to reimburse the pharmacy and the amount the PBM will charge the plan sponsor. These steps are known as "claims adjudication."

b. Who Owns PBMs?

There are independent, national PBMs, but there are also regional PBMs. In addition, some retail chains operate PBMs. Health insurers also operate PBMs; and, although some insurance companies provide PBM services only to their insurance clients, others market PBM services independently to pharmaceutical plan sponsors.

c. Customers of PBMs

The customers of PBMs are employers that provide prescription drug coverage as a benefit to employees, union health plans, insurers and government entities. Such customers contract with PBMs to manage the prescription drug benefit and contain the costs of that benefit. In the decade prior to 2002, "PBMs [came] to play a central role in administering prescription drug benefits in the private sector."[50]

d. Expanding PBM Offerings

(1) Maintain Retail Pharmacy Network

PBMs increasingly offer services to their customers beyond claims adjudication. PBMs create retail pharmacy networks to dispense prescriptions to plan members. Retail pharmacy networks typically include tens of thousands of independent and chain pharmacies, food chains, and mass merchandisers whose stores include pharmacy departments.

PBMs negotiate discounts from pharmacies that want to participate in the network. The negotiated price includes reimbursement for the cost of the drug plus a dispensing fee. Health plans that are willing to accept

50. CBO, ISSUES IN DESIGNING, *supra* note 4, at 14.

more restrictive pharmacy networks (networks with a more limited number of pharmacies) can achieve even greater discounts.[51] A study of three of the Federal Employees' Health Plans conducted by the General Accountability Office (GAO) showed that PBMs' negotiations with retail pharmacies have produced average discounts of 18 percent below the average cash price a customer would pay a retail pharmacy for 14 selected brand drugs and 47 percent below the average cash price for four selected generic drugs.[52]

PBMs do not purchase drugs from the manufacturer, unless the PBM operates a mail service pharmacy. Instead, the manufacturer sells drugs to a wholesaler, or directly to the retailer or mail service pharmacy. The retailer or mail service pharmacy pays the wholesaler or manufacturer and, in turn, is paid the price negotiated with the PBM through a combination of the patient's copayment and reimbursement from the PBM.

(2) Drug Utilization Review

PBMs run automated tests, known as drug utilization review, for plan eligibility, early refills, appropriateness of dosage, drug interactions, allergies, contraindications (e.g., age, sex, pregnancy), overutilization and fraud. These tests are performed electronically at the time of dispensing the pharmaceutical, when the pharmacist enters the patient's prescription in a computer.

51. U.S. GOV'T ACCOUNTABILITY OFFICE (GAO), FEDERAL EMPLOYEES' HEALTH BENEFITS: EFFECTS OF USING PHARMACY BENEFIT MANAGERS ON HEALTH PLANS, ENROLLEES, AND PHARMACIES 11 (Jan. 2003) [hereinafter GAO, FEDERAL EMPLOYEES' HEALTH BENEFITS], *available at* http://www.gao.gov/new.items/d03196.pdf.

52. *See id.* at 4; *see also* PHARM. CARE MGMT. ASS'N (PCMA), HOW PHARMACY BENEFIT MANAGERS HELP EMPLOYERS PROVIDE SAFER, MORE AFFORDABLE PRESCRIPTION DRUG BENEFITS 3 (Apr. 2005) [hereinafter PCMA, HOW PBMS HELP EMPLOYERS], *available at* http://pcmanet.org/assets/2008-03-25_Research_How%20PBMs%20Help%20Employers.pdf.

(3) Drug Formulary

A formulary is a list of drugs covered by the health plan. PBMs design formularies for their customers, and the customers can either select one of the PBMs standard formularies or have the PBM custom design a formulary. Typically, plan members pay lower copayments for drugs on the formulary than for drugs that are not on the formulary.

Formularies are generally organized by therapeutic category (a category includes drugs with the same indication,[53] although they may be chemically different). The formulary's therapeutic categories may be divided into tiers. Generics tend to be in the bottom tier, brand drugs on which the PBM has negotiated discounts or rebates from the manufacturer are in the middle tier, and the highest cost brand drugs are in the top tier. Plan members usually pay lower copayments for drugs in the lower tiers.

PBMs can administer graduated coinsurance rates, with the health plan paying the pharmacy a higher percentage of the prescription cost for preferred drugs than for nonpreferred drugs. Plan members pay the remainder.[54]

PBMs also have the capability of administering reference pricing systems. In reference pricing, the health plan pays the pharmacy a specified percentage of the full cost for a preferred drug, but for a nonpreferred drug, the health plan pays only a dollar amount equal to what it would pay for the preferred drug (the reference drug).[55] The plan member must pay the pharmacy the difference between the price of the nonpreferred drug and the plan's share of the price of the reference drug.[56]

53. The term "indication" means a specific use to treat a specific disease or condition. It has more formally been defined to mean "a symptom or particular circumstance that indicates the advisability or necessity of special medical treatment or procedure." MedlinePlus, http://www2.merriam-webster.com/cgi-bin/mwmednlm?book=Medical&va=indication.
54. *See* CBO, ISSUES IN DESIGNING, *supra* note 4, at 46.
55. *See id.*
56. *See id.*

(4) Pharmacy and Therapeutics Committee

PBMs often operate pharmacy and therapeutics (P&T) committees, which recommend which drugs to include on the PBMs formulary based on safety, efficacy, and clinical appropriateness. Once the P&T committee has assessed a drug, the PBM can place it in the appropriate tier of the formulary based on clinical and cost considerations.[57]

(5) Negotiate Prices with Manufacturers

PBMs negotiate prices with brand manufacturers.[58] The price reductions negotiated by PBMs frequently are in the form of rebates paid by the manufacturer to the PBM. Some or all of the rebates are passed through to the plan sponsor.[59] The portion of rebates that is passed through is subject to contract negotiation between the plan sponsor and the PBM.[60]

Rebates are related to the formulary. Manufacturers pay rebates for inclusion in the formulary and for market share, which is affected by the PBMs ability to use the formulary and incentives to steer drug usage.[61] Manufacturers are willing to pay larger rebates for more restrictive formularies (formularies with fewer drugs per therapeutic category).

(6) Promote Generic Use

PBMs develop strategies to stimulate generic use. PBMs advise plan sponsors of potential cost savings from generics, engage in generic substitution in their mail pharmacies, operate patient education programs, provide generic samples to physicians, and waive copayments to encourage patients to use generics.

57. *See* PCMA, HOW PBMS HELP EMPLOYERS, *supra* note 52, at 4.
58. *See* GAO, FEDERAL EMPLOYEES' HEALTH BENEFITS, *supra* note 51, at 1.
59. *See id.* at 4, 9.
60. *See id.* at 11.
61. *See id.* at 11-12.

(7) Promote Therapeutic Interchange

Therapeutic interchange is the substitution of one drug for another in the same therapeutic class where the two drugs are chemically distinct. PBMs contact physicians who have prescribed high-cost brand products to seek their authorization to use a lower-cost drug instead. There are two types of therapeutic interchange. The first involves obtaining authorization to dispense one brand drug instead of another brand drug, such as dispensing a brand drug on the formulary instead of a brand drug that is not on the formulary. The second involves obtaining authorization to dispense a generic that is on the formulary instead of a different branded drug.

(8) Step Therapy and Prior Authorization

Step therapy is the requirement that patients try less expensive drugs before the plan pays for a more expensive drug (and then only if the less expensive drugs are not effective). PBMs operate step therapy programs to contain the cost of the drug benefit.

PBMs operate prior authorization programs for certain drugs. Plan members may be required to obtain prior approval from the PBM before the pharmacist dispenses high-cost drugs, drugs with the potential for abuse, or nonformulary drugs.[62]

(9) Disease State Management

PBMs provide disease state management intervention programs for patients suffering from chronic diseases such as asthma, diabetes, hypertension, and depression. Such programs include patient and physician education and patient monitoring to ensure that patients receive appropriate medications and use them according to dosage instructions.

62. *See id.* at 13.

(10) Electronic Prescribing

Electronic prescribing systems provided by PBMs give physicians instantaneous electronic access to information about the patient's prescription history, formulary information, claims information, and mail service options. Such systems also permit physicians to transmit prescriptions electronically to a pharmacy. Electronic prescribing can improve the accuracy of information transmitted to the pharmacy and thereby improve patient safety,[63] increase formulary compliance, and foster generic substitution.

(11) Mail Service Pharmacy

PBMs can achieve savings for health plans through use of mail service pharmacies. Patients or physicians submit prescriptions by mail, fax, phone or the Internet to a mail service pharmacy. The mail service pharmacy dispenses the drug and sends it to the patient by mail or common carrier. Mail service pharmacies use automation to reduce the costs of dispensing prescription drugs. Mail service pharmacies dispense primarily medications for chronic (that is, ongoing) illnesses. They are less suitable for medicines for acute illnesses because of the time involved in delivering the drug.

Given that the mail service pharmacy has more time to dispense a drug than a retail pharmacist with the patient waiting at the pharmacy counter, mail service pharmacies can contact physicians to authorize therapeutic interchange or generic substitution for additional savings. For drugs examined in a GAO study of federal employee health plans that work with PBMs, the average mail service price was approximately 27 percent below the average cash price customers paid at a retail pharmacy for brand drugs and 53 percent below the average cash price customers paid for generic drugs.[64]

Plan sponsors encourage members to use mail service pharmacies by permitting the mail service pharmacy to dispense a 90-day supply of the

63. *See* PCMA, HOW PBMS HELP EMPLOYERS, *supra* note 52, at 7.
64. *See* GAO, FEDERAL EMPLOYEES' HEALTH BENEFITS, *supra* note 51, at 4.

drug for a single copayment, whereas a retail pharmacy is limited to dispensing a 30-day supply in exchange for a copayment.

Insurers and retail chains that operate PBMs either have their own mail service pharmacy or contract with an independent mail service pharmacy.

Total mail service distribution of prescription drugs, by independent mail service pharmacies and those owned by a PBM, insurance company, retail chain, or other owner, represented 17.2 percent of prescription dispensing in 2003.[65] In 2007, mail order pharmacies accounted for more than 20 percent of retail pharmacy sales.[66]

e. Specialty Drug Distribution

Specialty drugs are used to treat chronic or genetic diseases and disorders. Many specialty drugs are biologics. They are typically injected, infused, or inhaled.[67]

Specialty drugs tend to be developed for small patient populations.[68] Most specialty drugs are used to treat diseases that affect less than 3 percent of the population so that the volume of these drugs is low compared to traditional drugs.[69]

65. *See* FED. TRADE COMM'N, PHARMACY BENEFIT MANAGERS: OWNERSHIP OF MAIL-ORDER PHARMACIES, A FEDERAL TRADE COMM'N REPORT 16 (2005) [hereinafter FTC, PBMs: OWNERSHIP OF MAIL-ORDER PHARMACIES], *available at* http://www.ftc.gov/reports/pharmbenefit05/050906pharmbenefitrpt.pdf.
66. *See* Nat'l Ass'n of Chain Drug Stores (NACDS), 2007 Community Pharmacy Results [hereinafter NACDS 2007 Community Pharmacy Results], http://www.nacds.org/user-assets/pdfs/pharmacy/2007CommunityPharmacyResults.pdf (reporting IMS health data for year-end 2007 prescription drug sales and scripts, including sales and scripts from all retail pharmacies, including mail).
67. *See* PHARM. CARE MGMT. ASS'N (PCMA), SPECIALTY PHARMACY TRENDS AND MANAGEMENT STRATEGIES 5 (2006) [hereinafter PCMA, SPECIALTY PHARMACY TRENDS], *available at* http://www.pcmanet.org/assets/2008-03-25_Research_sp_trendsstrategies.pdf.
68. *Id.* at 3.
69. CURASCRIPT PHARMACY, 2004 SPECIALTY PHARMACY MANAGEMENT GUIDE & TREND REPORT 19 (2005), *available at* http://www.express-scripts.com/industryresearch/industryreports/specialtytrendreport/2004/strFinal.pdf

These drugs frequently require special handling, administration, patient education, and clinical support.[70] Many are shipped in special packaging to maintain the required temperature or require refrigeration.[71] Specialty drugs may be dispensed with related supplies to the patient or physician.

They also tend to cost more than traditional pharmaceuticals. "Annual treatment costs for patients requiring specialty pharmaceuticals are as high as $250,000, compared with an average of just $550 for those on traditional medications."[72]

To provide a sense of the significance of specialty drugs, in 2005, expenditures for specialty drugs totaled $55 billion, which was 24 percent of total drug expenditures.[73] Moreover, health expenditures for specialty drugs are growing at more than 20 percent per year, faster than for traditional drugs.[74]

Specialty drugs are distributed through retail pharmacies, mail service pharmacies, specialty pharmacies, physicians' offices, outpatient hospital facilities, and home infusion companies.[75] Some PBMs operate specialty pharmacies.[76]

Specialty pharmacies offer an array of services. They maintain inventory, provide distribution networks, and provide access to specialty pharmacists. These pharmacies work with patients to ensure that they take their medications consistently and in the proper dosage. Their staffs provide medication self-administration oversight, clinical assessment and patient monitoring, disease-state education, side-effect management, consultation with physicians, drug use review, formulary management,

70. *See* PCMA, SPECIALTY PHARMACY TRENDS, *supra* note 67, at 3.
71. *See id.* at 5.
72. PCMA, HOW PBMS HELP EMPLOYERS, *supra* note 52, at 7.
73. *See* PCMA, SPECIALTY PHARMACY TRENDS, *supra* note 67, at 4.
74. *See* Medco Health Solutions, Annual Report (Form 10-K), at 1 (Mar. 3, 2006).
75. *See* PCMA, SPECIALTY PHARMACY TRENDS, *supra* note 67, at 9.
76. Medco acquired Accredo Health Incorporated, a specialty pharmacy company, in 2005.

and therapeutic interchange. Specialty pharmacies coordinate nursing and social work services to educate, monitor, and support patients.

These pharmacies also manage billing and reimbursement.[77] Because specialty drugs are expensive and treat chronic diseases and conditions, cost and insurance coverage are concerns. Typically, the insurance provider is contacted before each shipment to determine the patient's insurance coverage. Employees of the specialty pharmacy review preauthorization and other approval requirements, lifetime limits, preexisting condition clauses, and the availability of state programs. They assist patients in obtaining alternate coverage if necessary. Patient care coordinators provide patient-assessment screening surveys at the time of each refill to identify high-risk patients and adverse clinical events.

f. PBM Compensation

PBMs may receive several forms of compensation. Plan sponsors pay administrative fees to PBMs for services such as drug use review, prior authorization programs, formulary development, and claims processing.[78] Also, PBMs may retain a portion of the rebates received from manufacturers. In addition to rebates, manufacturers pay PBMs fees for services such as data reporting, contacting physicians to change their prescribing patterns, and educating plan members about compliance with drug treatment plans.[79]

Plan sponsors can negotiate trade-offs in compensation with PBMs. For example, the plan sponsor may agree to pay administrative fees but insist that all the rebates from manufacturers be passed through.

PBMs have avoided assuming the insurance risk of the prescription drug benefit, except to a limited extent. They may receive a bonus or pay a penalty if they do not meet performance targets they negotiate with plan sponsors.[80] Performance targets include obtaining rebates on drugs, achieving levels of generic substitution, and overall cost savings.

77. *See* PCMA, SPECIALTY PHARMACY TRENDS, *supra* note 67, at 11.
78. *See* GAO, FEDERAL EMPLOYEES' HEALTH BENEFITS, *supra* note 51, at 26.
79. *See id.* at 27.
80. *See* CBO, ISSUES IN DESIGNING, *supra* note 4, at 14.

g. Medicare Part D Role

PBMs play various roles in the Medicare Part D program, which provides coverage for both brand-name and generic prescription drugs through Medicare Prescription Drug Plans, Medicare Advantage Plans, or other Medicare health plans that offer prescription drug coverage. They provide PBM services to health plans that have qualified to participate in the program. Through subsidiaries approved by the government, PBMs also offer the benefit directly to patients. Such subsidiaries must be risk-bearing entities regulated under state insurance statutes or similar laws. PBMs also collect and submit eligibility and drug cost data to the Centers for Medicare & Medicaid Services (CMS) on behalf of employers, unions and other health plans that qualify for the retiree drug subsidy available under the program.

5. Group Purchasing Organizations

A group purchasing organization (GPO) is an entity that engages in joint purchasing on behalf of its members from vendors of health care products, including pharmaceuticals and medical/surgical supplies, as well as office equipment.[81] In the health care setting, hospitals, nursing homes, home health agencies, pharmacies, and other providers participate in GPOs in order to realize savings and efficiencies that can be achieved through the aggregation of purchasing volumes. The types of savings and efficiencies that many health care providers obtain include access to volume discounts and reduced transaction costs, as well as consulting advice.[82] GPOs are reported to save their members—

81. *See* Press Release, Health Indus. Group Purchasing Ass'n (HIGPA), New Study Indicates Health Care Group Purchasing Provides Cost Savings of up to $38.7 Billion for U.S Hospitals (June 20, 2005), *available at* http://www.higpa.org /pressroom/2005/06-20-2005.asp.
82. *See* HIGPA, About HIGPA [hereinafter HIGPA FAQs], http://www.higpa.org/about/about_faqs.asp; U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, STATEMENTS OF ANTITRUST ENFORCEMENT POLICY IN HEALTH CARE, Statement 7 (1996) [hereinafter HEALTH CARE STATEMENTS], *available at* http://www.ftc.gov/bc/healthcare/industryguide/policy/statement7.htm.

particularly hospitals and free-standing nursing homes—between 10 percent and 15 percent off their purchasing costs.[83]

a. Origins of GPOs

According to the Health Industry Group Purchasing Association (HIGPA), GPOs have been in existence for purposes of hospital purchasing since as early as 1909, "when the Hospital Superintendents of New York first considered establishing a purchasing agent for laundry services."[84] Since then, the number and significance of GPOs have increased. During the 25 year period between 1974 and 1999, GPOs grew in number from 40 to more than 600.[85] Today, there continue to be in excess of 600 GPOs, with about 30 of them operating at the national level and the remaining negotiating contracts with regional vendors.[86]

The existence of GPOs—and the use of joint purchasing techniques—is not limited to the private sector health care field. The federal government, including the Department of Defense (DOD), General Services Administration, and the Department of Veterans' Affairs (VA), routinely use joint purchasing for health care products.[87] Joint purchasing arrangements are also common in many other sectors of the economy.

b. GPO Size, Structure, and Ownership

Not all GPOs are alike. Many differ in size, structure, and ownership. There are small, mid-size, and large GPOs. Some GPOs negotiate contracts with vendors of every type, thereby providing members with access to nearly every type of health care product,

83. *See* HIGPA FAQs, *supra* note 82.
84. *See id.*
85. *See* DEP'T OF JUSTICE & FED. TRADE COMM'N, IMPROVING HEALTH CARE: A DOSE OF COMPETITION, ch. VII, at 36 (2004) [hereinafter A DOSE OF COMPETITION, ch. VII], *available at* http://www.usdoj.gov/atr/public/health_care/204694.pdf; HIGPA FAQs, *supra* note 82.
86. *See* HIGPA FAQs, *supra* note 82; A DOSE OF COMPETITION, ch. VII, *supra* note 85, at 36.
87. *See* HIGPA FAQs, *supra* note 82.

whereas others focus solely on a particular product type.[88] Some GPOs are organized exclusively to serve not-for-profit providers, while others serve only proprietary entities, and still others serve any type of entity, regardless of how it is organized under corporate laws.[89] Some GPOs are owned by their members, while others have no ownership ties to their members.[90]

c. Members of GPOs

In the health care field, hospitals are important members of GPOs. Indeed, HIGPA has reported that approximately 96 percent to 98 percent of all hospitals participate in GPOs and 72 percent of hospital purchases are made through the use of GPO contracts.[91] According to HIGPA estimates, hospitals "use, on average, at least two and as many as four GPOs per facility" to obtain purchasing efficiencies.[92] GPOs serve many others in the health care field, including nursing homes, clinics, home health care agencies, physician practices, and pharmacies.[93]

d. GPO Services

The principal service offered by GPOs to their members is the negotiation of contracts for medical supplies, which, for some GPOs, can include pharmaceutical products.[94] In addition to group purchasing, GPOs may offer product-comparison analyses, standardization of

88. *See id.*; A DOSE OF COMPETITION, ch. VII, *supra* note 85, at 37.
89. *See* HIGPA FAQs, *supra* note 82.
90. *See id.*
91. *See id.*
92. *See id.*
93. *See id.*; A DOSE OF COMPETITION, ch. VII, *supra* note 85, at 37.
94. GPO members typically have purchasing selection committees comprised of health care professionals who determine which products or services are clinically appropriate. GPOs negotiate contracts based on each member's identification of desired goods and services. *See* HIGPA FAQs, *supra* note 82.

products, educational services, and purchasing technologies, as well as access to rebates and surplus dividends.[95]

In the pharmaceutical arena, GPOs negotiate with pharmaceutical manufacturers, wholesalers, and other vendors. GPOs do not purchase or obtain custody of the pharmaceutical products. Instead, these organizations act as buyers' agents, which negotiate contracts that all members of the GPO can access. Once a GPO contract is negotiated, GPO members purchase products directly from the manufacturer, wholesaler, or other vendor, at prices, terms, and discounts negotiated by the GPO.[96] Independent pharmacies join GPOs in order to obtain discounts by aggregating their purchases so that they can match chain pharmacies in the costs of their purchases and be able to survive in competition with chains.

To achieve volume discounts and other pricing efficiencies for its members, GPOs employ a number of contracting strategies. These generally include sole source contracts, commitments, bundling, and long-term contracts.[97] There has been significant debate about the propriety of such strategies from an antitrust perspective.[98]

95. *See* A DOSE OF COMPETITION, ch. VII, *supra* note 85, at 43; *see also* HIGPA FAQs, *supra* note 82.
96. *See* A DOSE OF COMPETITION, ch. VII, *supra* note 85, at 36; *Dep't of Justice & Fed. Trade Comm'n Health Care Competition Law and Policy Hearing on Group Purchasing Organizations*, at 127 (Sept. 25, 2003) [hereinafter *GPO Hearing*] (Statement of Robert E. Bloch, Mayer, Brown, Rowe & Maw).
97. *See Group Purchasing Organizations: Use of Contracting Processes and Strategies to Award Contracts for Medical-Surgical Products: Hearing Before the Subcomm. on Antitrust, Competition Policy and Consumer Rights of the S. Comm. on the Judiciary*, 108th Cong. 5-6 (2003) [hereinafter *GAO Senate Testimony*] (statement of the U.S. GAO).
98. *See, e.g.*, DOSE OF COMPETITION, ch. VII, *supra* note 85, at 38-46. *See generally* HERBERT HOVENKAMP, GROUP PURCHASING ORGANIZATION (GPO) PURCHASING AGREEMENTS AND ANTITRUST LAW (2004) (prepared for HIGPA), *available at* http://www.higpa.org/pdf/2004HovenkampGPO sandAntitrustLaw.pdf; *GAO Senate Testimony*, *supra* note 97.

(1) Sole Source Contracts

Sole source contracting occurs when a GPO negotiates to select one manufacturer to sell a particular product or set of products to the members of a GPO.[99] Sole source contracts with manufacturers enable GPOs to select as preferred the lowest bidding manufacturer for particular products desired by GPO members.[100] Notably, the exclusivity of the sole source contract with the manufacturer does not generally impact the GPO members' options. This is because most GPO contracts today do not require members to purchase goods exclusively through one GPO.[101] As a result, health care providers are free to participate in numerous GPOs and purchase products through the GPO contracts that provide the most efficient returns to the providers. Additionally, most GPO contracts offer relatively easy termination terms, allowing members to terminate participation upon 60 to 90 days' notice.[102]

In addition to sole source contracts, some GPOs offer dual or multisource contracts that allow members to buy products from competing manufacturers.[103]

(2) Commitments

GPO contracts can contain commitments to impose certain purchasing requirements on members of the GPO. Commitments can involve:

- the provision of heightened discounts upon the member's purchase of a specified percentage of products; and
- tiering, which enables the GPO member "to commit to different percentages of purchasing volume: the higher the percentage, the lower the price."[104]

99. *See GAO Senate Testimony*, *supra* note 97, at 5.
100. *See GPO Hearing*, *supra* note 96, at 130.
101. *See id.* at 130.
102. *See id.* at 41.
103. *See id.* at 130.
104. *GAO Senate Testimony*, *supra* note 97, at 5.

Volume is a significant factor affecting the ability of GPOs to obtain discounts. As a result, obtaining purchase volume commitments from members is an important mechanism for securing price concessions from vendors.[105] Some GPOs terminate members who do not satisfy commitment targets.[106]

(3) Bundling

GPO contracts that include "bundling" offer discounts conditioned on the purchase of a group of products. Product groups might comprise various products from one manufacturer or from multiple manufacturers.[107] Some bundles contain wholly differentiated products, some include complimentary items, and others involve products for which there are commitment-level requirements.[108] In 2003, the GAO identified a decrease in the use of bundles by GPOs.[109]

With regard to pharmaceutical products, some GPOs negotiate contracts that include bundles of generic and branded pharmaceuticals.[110] These bundles provide an opportunity for GPO members to obtain discounts on branded pharmaceutical products that they might not otherwise be able to secure.[111]

(4) Long-Term Contracts

Some GPOs negotiate long-term contracts (i.e., five years or more) with manufacturers, distributors, and other vendors. Such contracts may be subject to automatic renewal. Long-term contracts can be used to lock in favorable contract terms with manufacturers and, in turn, to

105. *See id.* at 12.
106. *See id.* at 13.
107. *See id.* at 6.
108. *See id.* at 13.
109. *Id.* at 14.
110. *See GPO Hearing*, *supra* note 96, at 156 (statement of John W. Strong, Consorta, Inc.).
111. *See id.* at 156.

"direct business to [such] manufacturers" for such periods.[112] According to the GAO, the use of long-term contracts by GPOs appears to be declining.[113]

e. GPO Compensation

In general, GPOs are paid by the vendors with which they contract. GPOs charge vendors administrative fees that often are based on the purchase price the health care provider pays for a product purchased through the GPO contract.[114] Specifically, the fees often are calculated as a percentage of each customer's purchases of products included within the GPO contract.[115] The fees are earned by the GPO each time a member purchases a product. The fees "cover a GPOs operating expenses and serve as its main source of revenue."[116] GPOs may distribute excess fees to members.[117]

6. Purchasers

Purchasers of pharmaceutical products include pharmacies, hospitals and clinics, health plans/insurers and PBMs that operate mail service pharmacies, and government buyers. These purchasers buy and obtain physical custody of pharmaceutical products through contracts with manufacturers, wholesalers, and GPOs. Purchasers make such products available for acquisition by individuals OTC or pursuant to a prescription or order written by an authorized health care practitioner.

112. *See GAO Senate Testimony*, *supra* note 97, at 5.
113. *See id.* at 14.
114. *See* HIGPA FAQs, *supra* note 82.
115. *See GAO Senate Testimony*, *supra* note 97, at 5.
116. A DOSE OF COMPETITION, Ch. VII, *supra* note 85, at 37; *GAO Senate Testimony*, *supra* note 97, at 5.
117. *See* A DOSE OF COMPETITION, Ch. VII, *supra* note 85, at 37; *GAO Senate Testimony*, *supra* note 97, at 5.

a. Pharmacies

Pharmacies are significant participants in the pharmaceutical marketplace. In 2008, there were nearly 74,000 pharmacies in the United States.[118] In 2007, more than 3.5 billion prescriptions were filled in the United States and pharmacies accounted for over $259 billion in sales.[119]

Consumers have a number of options for filling prescriptions. Specifically, they may choose between traditional "mom and pop" independent stores, regional and national chain drugstores, mass merchandisers, supermarket pharmacies, and mail order pharmacies. Still other types of pharmacies, which generally cater to more specialized populations, include long-term care pharmacies, specialty pharmacies, and Internet pharmacies.

Pharmacies purchase drugs from manufacturers and wholesalers. Some pharmacies—mostly larger chain stores, mass merchandisers, and supermarkets—negotiate directly with the manufacturers and wholesalers. Small independent pharmacies often participate in GPOs, which negotiate with the manufacturers and wholesalers on behalf of members. Whether negotiation occurs directly with manufacturers and wholesalers or through a purchasing agent (including a GPO), negotiation for pharmaceutical products focuses on obtaining volume discounts and rebates.[120]

118. *See* Nat'l Council of Prescription Drug Programs (NCPDP), New Pharmacy Database, http://www.ncpdp.org/provider_new_pharmacy_database.asp. NCPDP issues provider identification numbers to licensed pharmacies in the United States and its territories. *See* NCPDP Provider ID Number, Frequently Asked Questions—Pharmacy (2006), http://www.ncpdp.org/PDF/Provider_faq.pdf. The provider number is used by health plans, claims processors, clearinghouses, and other entities to identify pharmacies. *See id.* Each licensed pharmacy in the United States and its territories is eligible to apply for a NCPDP provider identification number. Most pharmacies have a NCPDP provider identification number.
119. *See* NACDS 2007 Community Pharmacy Results, *supra* note 66, at 3.
120. THE HEALTH STRATEGIES CONSULTANCY, LLC, FOLLOW THE PILL: UNDERSTANDING THE UNITED STATES COMMERCIAL PHARMACEUTICAL SUPPLY CHAIN 2, 19 (2005) (prepared for The Kaiser Family Foundation) [hereinafter FOLLOW THE PILL], *available at* http://www.kff.org/rxdrugs/upload/follow-The-Pill-Understanding-the-U-S-Commercial-Pharmaceutical-Supply-Chain-Report.pdf.
121. *See id.* at 9.
122. *Id.*
123. *See* NACDS 2007 Community Pharmacy Results, *supra* note 66, at 4.
124. *See* NAT'L ADVISORY COMM. ON RURAL HEALTH AND HUMAN SERVS., THE 2006 REPORT TO THE SECRETARY: RURAL HEALTH AND HUMAN SERVICES ISSUES 16 (2006), *available at* http://ruralcommittee.hrsa.gov/NAC06A Report.htm.
125. *See id.*
126. *See* NACDS 2007 Community Pharmacy Results, *supra* note 66, at 4.

Once pharmaceutical products are purchased, pharmacies take physical custody of the products and dispense them directly to consumers. Pharmacies must adhere to safe storage and dispensing requirements, which are governed by federal and state laws.[121] Pharmacy services include, among other things, "maintaining an adequate stock of pharmaceutical products, providing information to consumers about safe and effective use of prescription drugs, and facilitating billing and payment for consumers participating in group health benefit plans."[122]

(1) Independent Pharmacies

Independent pharmacies accounted for over 18 percent of prescription drug sales in 2007.[123] Independents, even those in rural areas, have faced increasing competition from larger chain, mass merchandiser, and mail order pharmacies.[124] Because price negotiation with manufacturers and wholesalers largely depends on purchase volumes, low sales volumes that typify independents, particularly rural pharmacies, pose an obstacle to obtaining the price advantages enjoyed by other types of pharmacies, particularly chain, mass merchandiser, and mail order pharmacies.[125]

(2) Chain Pharmacies, Food Stores, and Mass Merchandisers

Chain drugstores, food stores, and mass merchandiser pharmacies accounted for more than 61 percent of retail pharmacy sales in 2007.[126]

With more than 40 percent of these sales, chain drugstores constitute a significant competitive force in pharmaceutical distribution.[127] Food stores accounted for 11 percent of sales, and mass merchandisers accounted for 9.9 percent.[128] Pharmacies integrated into food stores sell a variety of medical and nonmedical goods and services.

(3) Mail Order Pharmacies

Mail order pharmacies are discussed supra in part 4.d.11.

(4) Long-Term Care Pharmacies

Long-Term Care (LTC) pharmacies are specialized retail pharmacies that provide prescription drug services to residents of nursing homes, assisted living facilities, hospice programs, and other institutional facilities. According to the Long Term Care Pharmacy Alliance (LTCPA), three major national LTC pharmacies serve more than 1.2 million people, accounting for more than three out of every five LTC facilities.[129] These three national LTC pharmacies dispense prescriptions through a network of more than 500 pharmacies nationwide.[130]

LTC pharmacies offer distinct services from retail pharmacies. In particular, LTC pharmacies develop formularies for the institutions they serve, "employ consultant pharmacists who conduct monthly drug regimen reviews for each resident at a facility to assess the appropriateness and efficacy of the drug therapies," provide packaging for controlled administration of drugs, and provide quality assurance checks, emergency drug kits and medication carts, regular and emergency delivery services, and in-service educational programs for health care professionals.[131]

Like large chain pharmacies, LTC pharmacies negotiate with manufacturers and wholesalers for rebates, and manufacturers, in turn,

127. *See id.*
128. *See id.*
129. *See* Long Term Care Pharmacy Alliance (LTCPA), LTCPA FAQ, http://www.ltcpa.org/mission/default.asp.
130. *See id.*
131. *Id.*; FOLLOW THE PILL, *supra* note 120, at 13, 20.

negotiate with LTC pharmacies for inclusion of their products on the LTC pharmacies' formularies.[132] LTC pharmacies purchase pharmaceutical products through direct manufacturer contracts, GPO contracts, and, increasingly, wholesaler contracts.[133]

(5) Specialty Pharmacies

Specialty pharmacies are discussed supra in part 4.e.

(6) Internet Pharmacies

Internet pharmacies sell prescription drugs directly to consumers. According to the GAO, there are three general types of Internet pharmacies.[134]

The first type, which often is associated with chain drugstores, requires consumers to present a prescription, as at regular drugstores, and offers a wide range of pharmaceutical products.[135] The second type offers a more limited set of products—often so-called lifestyle medications.[136] These pharmacies ask consumers to answer an "online medical history questionnaire" and, upon review of the information, physicians affiliated with the pharmacy issue a prescription for the requested medication, which the Internet pharmacy then fills.[137] The third type of Internet pharmacy dispenses medications without requesting a prescription.[138]

132. FOLLOW THE PILL, *supra* note 120, at 20-21.
133. *See* Health Strategies Group, Institutional Provider Systems, Long-Term Care Industry Trends and Drug Category Profiles, Research Summary (2006), *available at* http://www.healthstrategies.com.
134. *See* U.S. GOV'T ACCOUNTABILITY OFFICE, INTERNET PHARMACIES, SOME POSE SAFETY RISKS FOR CONSUMERS: REPORT TO THE CHAIRMAN, PERMANENT SUBCOMM. ON INVESTIGATIONS OF THE S. COMM. ON GOVERNMENTAL AFFAIRS 8 (2004).
135. *See id.*
136. *See id.*
137. *See id.*
138. *See id.*

There has been significant attention over recent years regarding sales of prescription drugs through the Internet and importation of drugs from Canada (and other countries) into the United States. Concerns regarding the sale of drugs via the Internet include safety and quality issues, including counterfeit and contaminated drugs, and unlawful diversion of prescription drugs.[139] In 2003, sales of drugs imported from Canada totaled approximately $700 million, or 0.3 percent of 2003 U.S. prescription drug sales.[140] Data from more recent years, however, reflect a significant decrease in Internet sales by Canadian pharmacies into the United States. Specifically, 2005 sales recorded by Canadian Internet pharmacies to U.S. consumers were approximately $420 million, and in 2006, only $211 million.[141] The decrease is attributed to various factors, including manufacturer-implemented supply restrictions, as well as negative press coverage concerning counterfeit drugs.[142]

b. Hospitals and Clinics

In addition to the pharmacies discussed above, hospitals and clinics often operate outpatient retail and inpatient pharmacies. Hospitals often purchase prescriptions from wholesalers or through GPO contracts.

139. Christie Provost Peters, Consultant, Nat'l Health Policy Forum Background Paper, Fundamentals of the Prescription Drug Market 17 (2004) [hereinafter NHPF Background Paper], http://www.nhpf.org/library/background-papers/BP_RxIndustry_ 08-24-04.pdf.
140. *See* THE KAISER FAMILY FOUND., PRESCRIPTION DRUG TRENDS 4 (2006) [hereinafter KFF, PRESCRIPTION DRUG TRENDS], *available at* http://www.kff.org/rxdrugs/upload/3057-05.pdf.
141. *See* Press Release, IMS Health Canada, Canadian Internet Pharmacy Sales to the United States Down 50 Percent in 2006 (Mar. 21, 2007), *available at* http://www.imshealthcanada.com/vgn/images/portal/cit_40000873/7/25/80533297IMS%20Release%20Final%20English.pdf.
142. *See id.*

c. Health Plans/Insurers

Health plans/insurers and PBMs are involved in the distribution of pharmaceutical products to consumers through their mail service pharmacies. Independent PBMs also operate mail service pharmacies.

d. Government Buyers

The government—through a number of agencies—purchases pharmaceutical products directly from manufacturers in order to dispense products to a variety of populations. The discussion of government buyers is included below in Section 7(b), which covers government third-party payors.

7. Third-Party Payors

Third-party payors—including self-insured employers and union health plans, private insurers, and government payors—are significant participants in the marketplace for pharmaceutical products because health insurance is a key factor in the extent and scope of access to such products.[143] In general, people with health care insurance "have greater prescription expenses than people without insurance."[144] Whereas uninsured individuals pay full retail price, people with insurance are able to purchase pharmaceutical products without actually paying the retail price of the medication. In addition, because insurers typically pay for the majority of the medication, and enrollees pay only a copayment or deductible, insured individuals generally do not know the price of the medication. Under this payment model, insured individuals (in contrast to uninsureds) are less likely to select among products based on cost.[145] As a result of this price insensitivity, third-party payors focus on, and have their greatest impact on, efforts to contain costs.

Some employers and union health plans elect to self-insure rather than use a health insurance company to offer health benefits to their

143. *See* KFF, PRESCRIPTION DRUG TRENDS, *supra* note 140, at 16.
144. *Id.*
145. *See id.*

employees. Such employers and union health plans tend to contract with PBMs to manage their prescription drug benefits.

a. Private Health Insurers

Health insurers assume the financial risk of prescription drug coverage in return for premiums paid by employers, union health plans, and individuals. Health insurers design plans to provide prescription drugs to members. Some health plans use a PBM, either their own or an independent, and the PBM provides services described in Section 4. Here, the discussion will focus on health insurers that do not use a PBM.

Health insurers generally do not purchase pharmaceutical products. Instead, pharmacies and other dispensers of pharmaceutical products contract with health plans for participation in the health plan's network of providers. Negotiated into the contracts are the fees the plan agrees to pay for the pharmaceutical products and the cost of dispensing those products.

In designing benefit packages, health plans make decisions regarding whether and to what extent to cover pharmaceutical products. Coverage decisions generally are made by pharmacy and therapeutics (P&T) committees, such as discussed above in the context of PBMs. P&T committees are comprised of physicians, pharmacists, and other professionals who examine clinical information regarding pharmaceutical products that have indications for the same condition. If the P&T committee decides to cover a particular pharmaceutical product, the health plan may include the product on its formulary. Noncovered drugs are excluded from the health plan formulary.

Decisions regarding the extent of coverage of pharmaceutical products are reflected not only by placement on the formulary, but also by the use of utilization management programs, or "preference systems."[146] A utilization management program or preference system is comprised of various rules applied to the formulary that are designed to give incentives to enrollees to use products identified by the health plan

146. *See* CBO, ISSUES IN DESIGNING, *supra* note 4, at Appendix A: Formulary-Based Strategies for Cost Control Used in the Private Sector.

as "preferred."[147] Common rules include, for example, tiered copayments, step therapies, prior authorization, graduated coinsurance rates, and reference pricing. These rules are similar to those used by PBMs, as discussed above.

Notably, some manufacturers offer rebates to health plans to help ensure that their products are included on a plan's formulary of drugs.[148]

b. Government Payors

As noted above, the government is a significant purchaser of pharmaceutical products. Government expenditures on pharmaceutical products most often are associated with public benefit programs covering specific populations. For example, the Department of Health and Human Services (HHS) administers—through CMS—the Medicaid program for low-income and certain medically-needy populations and the Medicare program for the elderly and disabled populations.[149] The VA acquires

147. *See id.*

148. *See id.*

149. HHS also administers—through the Health Resources and Services Administration—the 340B drug pricing program for at-risk populations. Section 340B of the Public Health Services Act requires manufacturers who participate in the Medicaid program to enter into contracts with HHS. Under these agreements, manufacturers must provide discounts on pharmaceutical products to Public Health Services "covered entities," such as certain disproportionate share hospitals, federally qualified health centers, state-operated AIDS drug assistance programs, public primary care clinics, community mental health centers, homeless clinics, and other safety net providers that do not have access to the Medicaid Drug Rebate program. (This program is discussed in Section 8(b)(1).) Prices achieved through the 340B discounts include a "minimum discount of 15.1 percent of AMP for brand name drugs and 11 percent of AMP for generic and OTC drugs." DAWN GENCARELLI, NAT'L HEALTH POLICY FORUM ISSUE, BRIEF NO. 807: ONE PILL, MANY PRICES: VARIATION IN PRESCRIPTION DRUG PRICES IN SELECTED GOVERNMENT PROGRAMS 10 (Aug. 29, 2005) [hereinafter NHPF ISSUE BRIEF], *available at* http://www.nhpf.org/library/issue-briefs/IB807_DrugPricing_08-29-05.pdf. Covered entities are not required to accept 340B discount pricing and may negotiate on

and pays for products for veterans who receive medical care from VA hospitals and clinics. Other agencies, including the DOD, Coast Guard, and Indian Health Service, also make expenditures for pharmaceutical products.

Medicaid and Medicare programs and the VA are the primary government buyers of pharmaceutical products. As discussed below, each of these programs acquires products from manufacturers at a discount, and they each have unique reimbursement methodologies that ultimately rely on, and arguably affect, price competition for pharmaceutical products.

(1) Medicaid Program

Medicaid is the joint federal-state medical assistance program for low-income Americans. As of 2006, more than 58.7 million individuals were enrolled in the program.[150] Under the Medicaid program, pharmacies and hospitals acquire pharmaceutical products through the above-described retail channels. The program covers the cost of prescription drugs in all states for beneficiaries of the program. Historically, Medicaid has been the largest public payor of outpatient prescription drugs.[151]

State Medicaid programs reimburse pharmacies for pharmaceutical products and pay a dispensing fee.[152] Medicaid enrollees pay nominal copayments, depending on the state, of up to three dollars per prescription. Reimbursement for pharmaceutical products is established through a formula determined by each state's Medicaid program. Most formulas reduce the average wholesale price (AWP) for brand products

their own to achieve larger discounts. *See id.*; NHPF Background Paper, *supra* note 139, at 28.

150. *See* Kaiser Family Foundation, Kaiser State Health Facts, Total Medicaid Enrollment, FY 2006, http://www.statehealthfacts.org/comparemaptable.jsp?ind=198&cat=4.

151. *See* KFF, PRESCRIPTION DRUG TRENDS, *supra* note 140, at 2.

152. For drugs used by hospital inpatients, Medicaid reimburses based on a flat fee for the inpatient stay or, if the drug is separately covered, on a drug-specific amount.

by a specific percentage—usually 10 percent to 16 percent.[153] For generic drugs, state Medicaid programs provide reimbursement based on the federal upper limit (FUL), the maximum allowable cost (MAC) of the drug, or AWP minus some percentage amount. FUL—which is set at 150 percent of the lowest-priced therapeutically and biologically equivalent drug—is used when a generic drug is sold by three or more different manufacturers.[154] MAC is a payment ceiling established by states for purposes of containing prescription drug costs. MACs may not exceed the FUL if a FUL has been established for a particular drug. Some states use a MAC for generic drugs when the MAC is lower than the FUL for a particular drug or when a drug does not yet have a FUL.[155] Because these formulas generally are based on AWP, Medicaid reimbursement formulas can benefit from price competition among manufacturers.[156]

In 1990, Congress—through the Omnibus Budget Reconciliation Act of 1990—created the Medicaid Drug Rebate program in order to help states control expenditures on pharmaceutical products. The program requires manufacturers to enter rebate agreements with the federal government in return for providing outpatient prescription coverage for the manufacturers' products through the Medicaid program.[157] The rebate agreement enables states to receive discounts that are similar to

153. *See* NHPF ISSUE BRIEF, *supra* note 149, at 6; CONG. BUDGET OFFICE, MEDICAID'S REIMBURSEMENTS TO PHARMACIES FOR PRESCRIPTION DRUGS 8 (Dec. 2004) [hereinafter CBO, MEDICAID'S REIMBURSEMENTS].

154. *See* CBO, MEDICAID'S REIMBURSEMENTS, *supra* note 153, at 8; *see also* CTRS. FOR MEDICARE & MEDICAID SERVS., FEDERAL UPPER LIMITS POLICY & REIMBURSEMENT (2005), http://www.cms.hhs.gov/Reimbursement/05_FederalUpperLimits.asp.

155. *See* CBO, MEDICAID'S REIMBURSEMENTS, *supra* note 153, at 9.

156. *See Medicaid Prescription Drugs: Examining Options for Payment Reform Sec. II(B), Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 109th Cong. (2005) (testimony of the NACDS).

157. *See* CTRS. FOR MEDICARE & MEDICAID SERVS., MEDICAID DRUG REBATE PROGRAM, OVERVIEW (2008) [hereinafter MEDICAID DRUG REBATE PROGRAM OVERVIEW], http://www.cms.hhs.gov/MedicaidDrugRebateProgram/.

those received by nonfederal purchasers. The rebate formula is based on two sets of prices: Average Manufacturer Price (AMP) and Best Price (BP). In general, "BP" is the lowest price available from the manufacturer to any wholesaler, retailer (pharmacies), provider (hospitals), health maintenance organization, and PBM.[158] The lowest price includes all cash discounts, free goods contingent upon any purchase requirement, volume discounts, and rebates. The Medicaid rebate under this program for brand name or innovator drugs is the difference between the manufacturer's AMP and BP for the product at issue.[159] The rebate for generic drugs is 11 percent of the AMP for the product at issue.[160] The existence of the Medicaid Rebate program may, in some instances, affect the extent and scope of price concessions offered by manufacturers for their products.

(2) Medicare Program

The Medicare program provides prescription drug coverage through the Part B outpatient benefit and, more recently, Part D outpatient prescription drug benefit.

(A) PART B

The Medicare Part B benefit covers a specific set of outpatient drugs, including self-administered drugs furnished in an outpatient setting, such as a physician's office, durable medical equipment drugs, certain drugs used by dialysis facilities, influenza drugs, pneumoccocal and hepatitis vaccines, antigens, hemophilia blood clotting factor, self-administered oral cancer and antinausea drugs, and immunosuppressive drugs.[161] Part B drugs are purchased by physicians and other providers. Medicare reimburses Part B drugs based on the manufacturer's average sales price (ASP).[162] ASP, which is a weighted average of actual prices paid (including pricing adjustments such as discounts and rebates), is

158. *See* 42 U.S.C. § 1396r-8(c)(1)(C)(i).
159. *See* MEDICAID DRUG REBATE PROGRAM OVERVIEW, *supra* note 157.
160. *See id.*
161. *See* 42 C.F.R. § 414.701.
162. *See id.* § 414.707.

proprietary information that manufacturers are required to report to CMS on a quarterly basis.[163]

(B) PART D

On January 1, 2006, the Medicare program implemented its Part D voluntary outpatient prescription drug benefit. Part D offers comprehensive coverage to 44 million Medicare beneficiaries.[164] As of February 2009, more than 26 million Americans have signed up for Part D coverage.[165] With the rollout of Part D, Medicare has assumed the mantle from Medicaid as the largest public buyer of prescription drugs.[166]

Medicare beneficiaries receive Part D coverage for brand name and generic drugs through two types of private health insurance plans, including fee-for-service type plans called prescription drug plans (PDPs) and HMO- or PPO-type plans called Medicare Advantage-prescription drug plans (MA-PDPs). The goal in using private plans reflects a market-based approach that provides beneficiaries choice among a range of plan options. As a result, the plans compete against each other—based on drug prices and formulary coverage—for Medicare beneficiary enrollment.[167]

In the same way as private plans, PDPs and MA-PDPs negotiate with pharmacies for product reimbursement and dispensing fees.[168] Plans may also negotiate with manufacturers for discounts and rebates, and CMS' expectation is that such negotiations will result in "comparable or better

163. *See id.* § 414.804.
164. *See, e.g.*, KAISER FAMILY FOUND., MEDICARE CHARTPACK 5 (2007), *available at* http://www.kff.org/medicare/upload/7710.pdf.
165. *See* CTRS. FOR MEDICARE & MEDICAID SERVS., 2009 ENROLLMENT INFORMATION, TOTAL MEDICARE BENEFICIARIES WITH PRESCRIPTION DRUG COVERAGE (2009), http://www.cms.hhs.gov/PrescriptionDrugCovGenIn/01_Overview.asp.
166. *See* NHPF Background Paper, *supra* note 139, at 24.
167. *See* Medicare Program, Medicare Prescription Drug Benefit, 70 Fed. Reg. 4193, 4298 (Jan. 28, 2005) (codified at 42 C.F.R § 423).
168. *See* 70 Fed. Reg. 4193, 4245.

savings than direct negotiations between the government and manufacturers."[169]

Payment amounts for pharmaceuticals through these insurance plans are determined through a competitive bidding process that requires plans to submit bids on an annual basis to CMS.[170] While plans base their bids on expected costs for an average Medicare beneficiary, CMS ultimately makes monthly prospective payments to plans based on the actual health status of plan enrollees. This payment system requires plans to control their costs so that actual expenditures per enrollee do not exceed the monthly payment amount. Controlling costs depends in large part on the use of formulary utilization management (or preference systems) and on obtaining price concessions from pharmacies and manufacturers. As a result, competition among manufacturers and wholesalers on the price of pharmaceuticals is a key aspect of the Part D program, as are the negotiations between and among plans, pharmacies, and manufacturers to obtain price concessions.

(3) Veterans Administration

The VA plays a significant role in the federal government's acquisition of pharmaceutical products because it accounts for a large percentage of the government's total prescription drug expenditures and it administers the Federal Supply Schedule (FSS).[171] The FSS is a list of more than 23 thousand pharmaceutical products, including brand name and generic drugs, and prices negotiated by the VA.[172] FSS prices generally are "equal to or lower than the price given to any of the drug manufacturer's nonfederal purchasers."[173] Other government agencies, such as the DOD and others referenced above, may purchase pharmaceutical products at the prices listed in the FSS.

Under federal law, manufacturers must participate in the FSS in order to gain access to the Medicaid prescription drug channel, which

169. *Id.*
170. *See* 42 C.F.R. § 423.251.
171. *See* NHPF Background Paper, *supra* note 139, at 27.
172. *See id.* at 27.
173. *Id.* at 11; *see also* FOLLOW THE PILL, *supra* note 120, at 25.

historically has comprised a significant percentage of total pharmaceutical sales in the United States.[174] Manufacturers must sell brand name products included on the FSS at the federal ceiling price (FCP), which is 24 percent below the AMP.[175] The discounts achieved by the VA can be "as much as 50 percent below the nonfederal AMP."[176] The VA also engages in competitive bidding for products that have therapeutic equivalents.[177]

B. Pharmaceutical Transactions and Distribution

Pharmaceutical distribution is complex and highly regulated at all levels of the distribution chain. These multiple layers of regulation, and their effects on the economic incentives of sellers and buyers, significantly affect antitrust analyses of pharmaceutical sales and distribution.

This section provides an overview of the wholesale and direct distribution of prescription and OTC drugs, including factors affecting price. The nature of the competition in pharmaceuticals is also discussed, focusing on competition through innovation of new active moieties[178]; through advertising and promotion, including direct-to-consumer (DTC) advertising and drug sampling; and through rebates and discounting, as influenced by formularies and reimbursement mechanisms established by governmental and private payors. Competition through introduction of generic drugs, including

174. *See* NHPF Background Paper, *supra* note 139, at 27.
175. *See* FOLLOW THE PILL, *supra* note 120, at 25; NHPF ISSUE BRIEF, *supra* note 149, at 11.
176. NHPF Background Paper, *supra* note 139, at 27.
177. *See* NHPF ISSUE BRIEF, *supra* note 149, at 11.
178. An active moiety is part of the active ingredient (without any salt or ester appendages that is responsible for action in the body (e.g., binding to an enzyme). 21 C.F.R § 314.108(a) ("*Active moiety* means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.").

mechanisms used by governmental and private payors to increase generic use, is also reviewed. Finally, competition involving OTC drugs, including switches from prescription to OTC status and the use of store brands, is discussed.

1. Prescription Drugs

The distribution and sale of prescription drugs proceed by various paths from manufacturer to patient. Manufacturers sell prescription drugs to a wholesale distributor, which, in turn, distributes to dispensing organizations, including retail and institutional health care providers. Although the vast majority of prescription pharmaceuticals are distributed through wholesalers, some larger dispensing organizations purchase products directly from the manufacturer. The dispensing organizations provide the pharmaceutical products to patients pursuant to physician prescriptions.[179]

Numerous factors in addition to the physician's diagnosis influence the choice of the drug prescribed and provided to the patient. These include insurance coverage limitations and other restrictions imposed by third-party payors, and pricing factors, such as availability of manufacturer discounts negotiated by certain health care providers and other entities. The following sections provides a brief overview of the distribution and marketing processes and regulations that influence distribution for drug products.

a. Wholesale Distribution

Pharmaceutical manufacturers ordinarily sell their prescription products through one or more wholesale distributors. These wholesalers, in turn, supply dispensing organizations, including retailers, such as drugstore chains, independent community pharmacies, and mass merchandisers, PBMs, and institutional health care providers, such as hospitals, physicians' offices, home health care providers, and clinics.

179. For ease of reference in this Handbook, we generally refer to prescribers as doctors or practitioners, but note that other types of health care practitioners (e.g., nurse practitioners) also may have the authority to prescribe drugs to patients.

Such institutional providers also have formed GPOs to obtain larger discounts.

Wholesale distribution can promote economic efficiencies and reduce costs by minimizing transaction costs.[180] For example, selling through wholesale distributors may enable the manufacturer to consolidate individual small-volume sales. Similarly, purchases from wholesalers can avoid the burden of dealing with several separate manufacturers.[181]

Prescription drug wholesale distribution generally occurs in one of three basic models.[182] First, a manufacturer may sell prescription products to large national distributors, or to smaller regional or specialized distributors, who sell directly to dispensing organizations.[183] Like the national distributors, regional distributors may offer a complete or nearly complete line of drug products to customers, but operate in a smaller geographic area and smaller product volumes.[184] Specialty distributors ordinarily focus on certain types of drug or biologic products, such as vaccines, which may require refrigeration.

Second, in a variation of the above system, large national or regional wholesalers may distribute to a smaller wholesaler, for distribution to dispensing entities.[185] These smaller wholesalers may service small independent pharmacies or physician offices, or also focus on product lines with special shipping requirements, such as parenterals (injectibles) or biologics.[186]

Third, manufacturers also may sell drugs at discounted prices to so-called secondary wholesalers.[187] As discussed, pharmaceutical companies offer discounted prices at various points during the year for a

180. 2003 HDMA INDUS. PROFILE, *supra* note 46.
181. FOOD AND DRUG ADMIN., PROFILE OF THE PRESCRIPTION DRUG WHOLESALING INDUSTRY, FINAL REPORT § 1.2 (Feb. 21, 2001) [hereinafter FDA, PROFILE], *available at* http://www.fda.gov/oc/pdma/report2001.
182. *Id.* § 1.50.
183. *Id.* §§ 1.5.1, 1.5.2.
184. *Id.* § 1.3.2.
185. *Id.* § 1.5.3.
186. *Id.* § 1.3.3.
187. *Id.* § 1.5.4.

variety of reasons,[188] and secondary wholesalers focus on purchasing such discounted volumes. To profit from the discounted price and recoup their capital investment, secondary wholesalers must resell the discounted drugs quickly.[189] This discounted drug distribution model may involve several transactions among wholesalers before the drugs are finally sold to the dispensing organization.[190]

In the past, drug manufacturers used inflation-based models to compensate primary (e.g., national) wholesalers for their distribution services.[191] For reasons described above, inflation-based compensation for primary distributors has gradually been phased out in recent years in favor of a fee-for-service compensation model.[192]

Distribution patterns generally are the same for both brand name and generic products, although generics are less frequently sold at discounted prices, as they are already priced significantly less than pioneer pharmaceuticals.[193] Generic products are thus less likely to be distributed through secondary wholesalers.[194]

b. Direct Distribution

Larger dispensing organizations, particularly chain drugstores and mass merchandisers, may purchase prescription drugs directly from the manufacturer rather than from a wholesaler. These organizations "self-warehouse" the product for distribution to their own retail pharmacy or store locations. In recent years, many retail chains have increased their reliance on self-warehousing.[195]

188. *See supra* text accompanying note 40.
189. FDA, PROFILE, *supra* note 181, § 1.3.4.
190. *Id.* § 1.5.4.
191. *See, e.g.*, AmerisourceBergen Co., Annual Report (Form 10-K), at 6 (Dec. 9, 2005) at 6-7; McKesson Corp., Annual Report (Form 10-K), at 9 (May 16, 2006); Cardinal Health, Inc., Annual Report (Form 10-K) at 6 (Sept. 1, 2006).
192. A discussion of inflation-based models is provided at part A.3.a of this Chapter.
193. FDA, PROFILE, *supra* note 181, § 1.6.1.
194. *Id.*
195. *Id.* § 1.5.1.

c. Factors Influencing Prescription Drug Choice

Dispensing organizations, including retail and institutional health care providers, provide prescription products to patients pursuant to a doctor's order. However, the doctor or pharmacist may first need to determine whether the patient's insurer or other third-party payor, including Medicare or Medicaid, has imposed any coverage limitations or other restrictions on reimbursement for particular drugs. Third-party payors may employ various restrictions to control prescription drug costs, including:

- Limiting coverage to specific products listed on prescription drug formularies;
- Requiring substitution of generic products for brand name products;
- Requiring substitution of lower cost drugs within the same therapeutic class, but that may differ in chemical composition (i.e., are not generic equivalents);
- Requiring physicians first to prescribe lower cost therapies before trying more expensive ones (step-care programs);
- Monitoring physician prescribing behavior using drug utilization review programs;
- Requiring prior authorization for coverage of high-cost therapies.[196]

In addition, mandatory substitution laws in some states require pharmacists to dispense generic alternatives to patients with a prescription for a brand name product.[197]

196. FED. TRADE COMM'N, THE PHARMACEUTICAL INDUSTRY: A DISCUSSION OF COMPETITIVE AND ANTITRUST ISSUES IN AN ENVIRONMENT OF CHANGE 31, 33 (1999) [hereinafter FTC PHARM. INDUS. REPORT], *available at* http://www.ftc.gov/reports/pharmaceutical/drugrep.pdf.
197. *See id.* at 18.

d. Factors Affecting Prices

Purchasers of large volumes of drugs, such as hospitals, GPOs, and PBMs, ordinarily negotiate volume-based price discounts or rebates from pharmaceutical manufacturers. Third-party payors, such as health insurers and PBMs, may also negotiate price discounts and reimbursement rates with drug companies and pharmacies, or use risk-sharing capitation programs,[198] which split any cost savings between the manufacturer and insurer if cost maximums are not exceeded. These negotiated price concessions occur directly between the provider and manufacturer, although the health care providers may still receive delivery of their products from wholesaler distributors.[199] In these instances, the wholesalers purchase the product from the manufacturer at the regular price, sell it to the health care provider at the negotiated discount price, then charge the price difference back to the manufacturer.[200] Some PBMs further manage prescription drug costs by dispensing products to patients directly, via Internet or mail order pharmacies. This enables the PBM to exercise more control over compliance with cost saving restrictions, such as adherence to its drug formularies, and use of generic and therapeutic equivalent substitution programs.

Most brand name prescription drug manufacturers have multiple tiers of prices, with differing discounts and allowances, for various types of purchasers. Manufacturers may have in excess of a dozen different pricing tiers, reflecting the different positions of purchasers in the distribution chain and their differing customer bases. These groupings, termed "classes of trade," include retail pharmacies, hospitals, GPOs, PBMs, home health care providers, government purchasers such as the VA, and others. Disfavored purchasers have occasionally challenged such discounts under Section 2(a) of the Robinson-Patman Act,[201] on the ground that they functionally compete with the favored purchasers for

198. *Id.* at 29.
199. *See* 2003 HDMA INDUS. PROFILE, *supra* note 46, at xii.
200. *Id.*
201. 15 U.S.C. § 13(a).

resale customers, though few such challenges have resulted in litigated decisions.[202]

2. *Over-the-Counter Drugs*

The distribution of OTC drugs differs significantly from that for prescription drugs, since OTC drugs can be purchased without the necessity of a physician visit or prescription. OTC drugs contain only active ingredients that are generally recognized as safe and effective (GRAS/E) or are listed in final monographs in the FDA's regulations, and that can be self-administered. Also, like prescription drugs, most OTC products are distributed by manufacturers through wholesalers. Moreover, there also can be two versions of OTC products: generic (store brands) and branded products. The latter are supported by consumer advertising and promotion. OTC drugs usually are not covered by insurers or other third-party payors and, because patients may purchase OTC products directly, physicians or other health care professionals provide much less influence over their selection than they do for prescription drugs.

C. Pharmaceutical Competition

Brand name pharmaceutical companies seek competitive advantage in a therapeutic category through various mechanisms, including innovation, patent promotion, and life cycle management. The following provides an overview of current pharmaceutical industry practices for the development and marketing of prescription and OTC drug products in the United States.

202. *See, e.g.*, Drug Mart Pharm. Corp. v. Am. Home Prods. Corp., No. 93-CV-5148, 2007 WL 4526618 (E.D.N.Y. 2007) (summary judgment granted; plaintiffs failed to demonstrate actual antitrust injury from the price differentials).

1. Prescription Drugs

Decisions on the choice of prescription drugs are not formally made by the ultimate purchaser of the drug (the patient).[203] Patients ordinarily rely on the determination of the prescriber, and generally lack sufficient medical knowledge or information on alternative therapies and their prices to evaluate these decisions on their own. Further, because patient costs for pioneer drugs are usually covered by health insurance or other third-party payors, patients and doctors lack financial incentives to choose potential alternative products based on price, absent controls (e.g. lower copays) or restrictions on drug choice imposed by payors.[204] Given these factors, pioneer prescription drug manufacturers historically have focused on characteristics other than price, such as promotion to doctors through specialized technical sales personnel, called "detail forces," and innovation of new therapies. However, in recent years, insurers and other third-party payors have sought to manage rising health care costs, particularly in the area of prescription drugs, by reducing or stabilizing pharmaceutical manufacturers' pricing through various mechanisms, including restricted formularies and prior approval requirements for prescribing brand name products when a generic version is available.

a. Innovation

Limited patent exclusivity periods, resulting in eventual generic competition, lead brand name pharmaceutical companies continually to develop new or improved (follow-on) products both to retain their

203. As an informal matter, patients have developed influence over prescribing choices through the development of DTC advertising of prescription drugs. *See* FED. TRADE COMM'N AND DEP'T. OF JUSTICE: A REPORT BY THE FEDERAL TRADE COMMISSION AND THE DEPARTMENT OF JUSTICE, IMPROVING HEALTH CARE: A DOSE OF COMPETITION, ch. VII at 19-21 (July 2004) [hereinafter A DOSE OF COMPETITION, ch. VII]. Physicians ordinarily give deference to patients' requests for specific products absent medical reasons to prescribe otherwise.

204. FTC PHARM. INDUS. REPORT, *supra* note 196, at 8.

current prescriber base and to expand into new therapeutic markets. Innovation in the pharmaceutical industry generally falls into two categories, as described by the Federal Trade Commission (FTC or Commission): (i) discrete innovation, which focuses on the discovery, development, and approval of new chemical/molecular or biological entities;[205] and (ii) incremental innovation, which encompasses enhancements to existing products,[206] such as new formulations, dosage forms, or new indications of use.[207]

Discrete innovation, leading to the marketing of novel therapeutic products, generally provides companies with the greatest financial rewards, particularly if no other effective treatment is available or the new product offers therapeutic advantages over other existing treatments. Discrete innovation also may enable companies to enter new markets, expand their presence in existing areas, or foster entry by start-up companies. Nearly all new chemical/molecular entity and biological products will qualify for some form of market exclusivity, whether de facto, by reason of the requirement that potential competitors obtain FDA marketing approval, as the result of an explicit legislative grant, e.g., patent, Hatch-Waxman non-patent exclusivity periods,[208] or because of pediatric[209] or orphan drug[210] exclusivity.

While the financial rewards from innovation can be very high, the financial risks associated with required research and development efforts are substantial. As discussed above, pharmaceutical innovation is an expensive, resource-intensive, time-consuming, and uncertain

205. FED. TRADE COMM'N, TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW AND POLICY, ch. 3, at 4-5 (2003), *available at* http://www.ftc.gov/os/2003/10/innovationrpt.pdf.

206. *Id.*

207. A DOSE OF COMPETITION, ch. VII, *supra* note 203, at 5.

208. Approved new drug applications (NDAs) for a new chemical entity may receive five years of exclusivity, and approved NDAs for a new condition of approval supported by clinical investigations conducted by or for the applicant may receive three years of exclusivity. 21 U.S.C. § 355(c)(3)(D)(ii)-(iii).

209. *Id.* § 355a(b)(c).

210. *Id.* § 360cc.

investment.[211] Even when a company is successful in screening, developing, testing (both preclinical and clinical), and obtaining FDA approval for a new drug, the company will face additional costs and risks associated with the commercial launch of the product, such as manufacturing scale-up (the transition for research to production volumes), new product promotion, and, increasingly, reimbursement categorization (obtaining from the Centers for Medicare and Medicaid Services coverage and reimbursement-level determinations for the product).

Incremental innovation usually entails less risk, because it builds on an already approved and successfully marketed product, reducing the uncertainty and cost of development. Examples of incremental innovation include developing a different, more convenient, dosage form or frequency of administration; an improved formulation, perhaps with lessened adverse indications or a combination product; and adding another drug to produce enhanced therapeutic effects. Enhancements to existing products can result in new, or extended, exclusivity under the applicable statutes. Switches of prescription drugs to over-the-counter status (Rx-to-OTC) are another mechanism potentially available for certain therapeutic classes of drugs to maintain some sales following loss of a drug's market exclusivity protection.[212] Such developmental efforts are often referred to as life cycle management. Incremental innovation may also be used to expand demand for existing drugs through research to support an expanded patient population (e.g., pediatrics), or new clinical indications.

b. Advertising and Promotion

Once a company has obtained FDA approval to market a new drug (whether a new chemical entity or an enhanced version of an approved drug), the company must educate doctors, pharmacists, medical researchers, and other health care professionals to promote acceptance, prescription, and use. Pharmaceutical product promotion is highly

211. *See* discussion *supra* part A.1.
212. *See* discussion *infra* Chapter II.A.3 (regarding OTC drugs and Rx-to-OTC switch).

regulated by the FDA. Virtually all drug advertising and promotion is focused on brand name products;[213] generic companies compete primarily on price, and do little or no promotion, relying on the efforts of third-party payors and state generic substitution laws. Promotion of brand name drugs focuses primarily on nonprice attributes of the product;[214] as explained, the prescribers and patients do not pay for the drugs (beyond a copayments), which are generally covered by third-party payors.

The FDA permits only very limited promotional efforts before a New Drug Application (NDA) approval. Investigational products can be promoted either through "institutional" advertisements or "coming soon" advertisements, but not both. Institutional advertisements may state that a company is conducting research in a particular therapeutic area, but may not identify a particular drug by name, suggest that the drug will soon be approved for the use under investigation, or make representations about the drug's mechanism of action or specific proposed intended uses. Coming soon advertisements may announce the name of a new product that will soon be available, but may not make representations or suggestions about the drug's safety, efficacy, or proposed intended use.

Following NDA approval, companies may promote pharmaceutical products using a variety of methods, including promotion to health care professionals, DTC print and broadcast advertisements, and pharmaceutical detailing visits to prescribers and managed care purchasing officials. The FDA closely regulates all of these forms of promotion. Pharmaceutical companies are required to submit advertisements and promotional labeling to the FDA at the time of initial dissemination.

Print advertisements and promotional labeling (those promotional materials provided to prescribers other than advertising in journals and other publications directed to health care professionals) directed to physicians may include brochures, press releases, booklets, mass-mailing pieces, bulletins, sales aids, price lists, catalogs, and Web sites, as well as ads placed in published journals, magazines, special advertising

213. FTC PHARM. INDUS. REPORT, *supra* note 196, at 187.
214. *Id.*

supplements, newspapers, and periodicals. Such materials must be consistent with FDA-approved labeling, and provide fair balance concerning the drug's benefits and risks, including a brief summary of risks.[215] Claims of superiority to or comparability with rival drugs are not permitted unless supported by substantial evidence or substantial clinical experience. In practice, this has meant that comparative clinical trials are required for such claims; in view of the substantial expense of such trials, few have been undertaken. In 2007, the National Institutes of Health announced the first government-funded comparative effectiveness clinical trial of prescription drugs. In view of increasing drug costs, there has been significant interest in recent years in the development of mechanisms to support comparative effectiveness research.[216]

Promotion of a drug product for indications not in the approved labeling, termed "off-label" promotion, is highly controversial and also restricted. Companies can, for example, provide health care professionals with certain information relating to off-label uses, such as unaltered peer-reviewed articles, or in response to unsolicited requests from medical professionals. More stringent FDA restrictions on the provision of truthful, scientific information were challenged as unconstitutional, and the FDA clarified its position in a series of decisions.[217] The FDA subsequently has not engaged in active enforcement concerning off-label promotion. Rather, the Department of Justice (DOJ) and the Office of the Inspector General (OIG) of HHS, under both the Federal False Claims Act[218] and the federal antikickback

215. 21 C.F.R. § 202.1.
216. *See, e.g.*, CONG. BUDGET OFFICE, RESEARCH ON THE COMPARATIVE EFFECTIVENESS OF MEDICAL TREATMENTS (Dec. 2007).
217. *See* Wash. Legal Found. v. Henney, 128 F. Supp. 2d. 11 (D.D.C. 2000), *remanded by* 202 F.3d 331 (D.C. Cir. 2000).
218. The False Claims Act prohibits knowingly presenting (or causing to be presented) to the federal government a false or fraudulent claim for payment or approval. 31 U.S.C. § 3729-3733. Additionally, it prohibits knowingly making or using (or causing to be made or used) a false record or statement to get a false or fraudulent claim paid or approved by the federal government or its agents, such as a carrier, other claims processor, or state Medicaid program.

statute,[219] as well as the states and private plaintiffs, have challenged off-label promotion regularly in recent years, alleging that reimbursement for such uses was unlawfully obtained.

Pharmaceutical companies also promote their products through their detail sales forces, including promotions at medical conferences, visits to hospitals, clinics, and physician offices, and product demonstration-informational meetings for industry thought-leaders. Promotional materials for prescription products are sometimes also directed toward pharmacists, to educate them about all the available options in a given therapeutic class, make them aware of newer products on the market, or alert them to risks of drug interactions that the prescribing physician might overlook or not anticipate because of unfamiliarity with the patient's current course of treatment.

In addition to advertisements directed toward health care providers, pharmaceutical companies also sometimes use DTC advertising for certain types of products. DTC advertising may include Internet ads and podcasting as well as more traditional methods, such as print, television, or radio advertisements. DTC advertising has been used to promote drugs that treat various conditions, including high cholesterol, depression, attention deficit disorder, and erectile dysfunction. Both the FTC and the FDA have been supportive of the positive effects of DTC advertising in providing additional information to consumers.[220] The FDA, for example, has observed that accurate consumer-directed or DTC prescription drug promotion "can lead to significant increases in the detection of under-treated conditions like high blood pressure, diabetes, and depression, with consequent health benefits for Americans,"[221] in addition to encouraging a general dialog between patients and their treating physicians that may not have existed previously.[222] DTC communications regarding prescription medicines also may facilitate

219. 42 U.S.C. § 1320a-7b(b).
220. *See* A DOSE OF COMPETITION, ch. VII, *supra* note 203, at 18-21.
221. *See FDA Regulates Prescription Drug Promotion: Hearing Before the S. Spec. Comm. on Aging*, 108th Cong. (2003) (statement by Janet Woodcock, M.D., Director, Ctr. for Drug Evaluation and Research, Food & Drug Admin.).
222. *Id.*

patients' compliance with treatment regimens.[223] The expense of DTC ads has, however, been a subject of criticism by some in Congress and managed care entities, as potentially contributing to increases in drug prices.

"Reminder" advertising, which provides information for and refers to a particular drug, and "disease-awareness" communications, which do not refer to a particular drug, are also commonly employed by pharmaceutical companies. Reminder ads may not make claims regarding the drug, but may feature only the brand (trademark) and generic (chemical) names of a drug, and are intended to create knowledge of the availability of newly approved drugs or increase or maintain recognition for an established product.[224] Formats of reminder ads can range from free pens or T-shirts bearing the product name to television commercials. These more limited vehicles are subject to lesser FDA restrictions and scrutiny than other types of promotional communications.

Disease awareness, or "help seeking," communications use a completely different marketing approach. These communications do not name a specific drug but, rather, only discuss a particular disease or health condition. FDA has acknowledged that disease awareness communications "can provide important health information to consumers and health care practitioners, and can encourage consumers to seek, and health care practitioners to provide, appropriate treatment."[225] Disease awareness communications are particularly valued by many health care professionals for their potential to bring attention to rare or under-treated health conditions.[226] Because they do not mention or promote a specific

223. *See* Pharm. Research & Mfrs. of Am. (PhRMA), Guiding Principles: Direct to Consumer Advertisements About Prescription Medicines 2 (2006), *available at* http://www.phrma.org/files/DTCGuidingprinciples.pdf.
224. 21 C.F.R. § 202.1(e)(2).
225. *See* FDA GUIDANCE FOR INDUSTRY: "HELP-SEEKING" AND OTHER DISEASE AWARENESS COMMUNICATIONS BY OR ON BEHALF OF DRUG AND DEVICE FIRMS (Draft guidance) 1 (2004), *available at* http://www.fda.gov/cber/gdlns/helpcomm.pdf. The FDA has not yet issued final guidance.
226. Because communications that properly may be considered disease awareness communications do not constitute product labeling or product advertisements, such communications are not subject to the risk disclosure and other such requirements under the Federal Food, Drug, and Cosmetics Act.

product, these communications are not subject to FDA requirements for prescription drug advertising.

c. Drug Sampling

Drug sampling is another key component of marketing and sales strategies for pharmaceutical products and refers to the provision of free drug samples[227] to a licensed practitioner for distribution to patients.[228] Drug sampling is regulated by both the FDA and the HHS OIG.

The Prescription Drug Marketing Act of 1987 (PDMA) (as modified by the Prescription Drug Amendments of 1992 (PDA) and the FDA Modernization Act of 1997) amended the Federal Food, Drug and Cosmetic Act (FDCA) to establish requirements concerning the marketing and distribution of prescription drugs.[229] The PDMA prohibits, with few exceptions, the sale, purchase, or trade of prescription drugs that were purchased by, or provided as samples to, hospitals or other health care entities.[230] Where sampling is permitted, the PDMA, and FDA's regulations promulgated thereunder, require that the manufacturer complete and maintain copies of detailed sample request[231] and receipt forms,[232] as well as conduct at least an annual inventory and reconciliation of all sample requests, distributions, thefts, and losses.[233]

227. "Drug sample" means a unit of a prescription drug that is not intended to be sold and is intended to promote the sale of the drug. 21 C.F.R. § 203.3(i).
228. 21 C.F.R. §§ 203.30-203.39.
229. Pub. L. No. 100-293 (Apr. 22, 1988).
230. 21 U.S.C. § 353(c)(1) (pertaining to drug samples); 21 U.S.C. § 353(c)(3)(A)(ii)(I) (pertaining to the resale of purchased drugs).
231. 21 C.F.R. § 203.30(a)(1), (b) (pertaining to sample distribution by mail or common carrier); 21 C.F.R. § 203.31(a)(1), (b) (pertaining to direct delivery by a company representative).
232. 21 C.F.R. § 203.31(c).
233. *Id.* § 203.31(d)(2).

The FDA's regulations require pharmaceutical manufacturers and distributors to ensure that samples are (i) distributed to an appropriate practitioner, pharmacy, or hospital (through verification of a valid state license); (ii) handled and stored in compliance with compendial (referring to any requirements as to handling imposed by the U.S. Pharmacopia's monograph for the particular drug) and labeling requirements; (iii) have proper forms and labeling; and (iv) have lot or control numbers recorded in an inventory. The FDA also requires that manufacturers and distributors investigate any falsification of records or diversion of product samples, and notify FDA of any such activity.[234] Further, the FDA requires manufacturers to establish and adhere to written policies and procedures describing administrative systems concerning sample distribution, storage, theft, inventory, and other relevant controls.[235]

Development of the procedures and systems necessary to meet the requirements of the PDMA and its implementing regulations is left to the discretion of manufacturers and their authorized distributors. The FDA periodically inspects a manufacturer or authorized distributor to review the company's record-keeping and sample security and examine its audit procedures. The FDA does not inspect individual practitioners, focusing instead on manufacturers and distributors.

In some circumstances, if samples have monetary value to the recipient (e.g., a physician) and are used to treat federal health care program beneficiaries (i.e., Medicare or other federal health care programs, such as those of the VA or the DOD, improper use of samples, including receiving reimbursement for their provision to federal beneficiaries, may also trigger liability under other statutes, primarily the False Claims Act[236] and the antikickback statute.[237] The OIG has listed elements "that have been widely recognized as fundamental to an effective [sales and marketing] compliance program," including, among other things, effective training and education programs, establishing an internal compliance officer, internal monitoring and enforcement, and

234. *Id.* §§ 203.31- 203.33, 203.37-203.38.
235. *Id.* § 203.34.
236. 31 U.S.C. §§ 3729-3731.
237. 42 U.S.C. § 1320a–7b(b).

enforcement of standards through well-publicized disciplinary procedures.[238] A manufacturer's noncompliance can invite scrutiny by the OIG, with potential criminal penalties, the possibility of debarment, and exclusion from government-reimbursed programs.

The distribution of controlled substances (primarily narcotic and other habit-forming drugs subject to abuse) is stringently controlled through regulations and enforcement by the Drug Enforcement Administration (DEA). The DEA requires manufacturers, distributors, pharmacies, and physicians to register with the DEA, comply with drug security regulations and maintain records of distribution.[239]

d. Pricing, Formularies, and Reimbursement

Increasing concerns regarding the level of prices of prescription drugs have led both government and private payors to develop various mechanisms to attempt to reduce costs by influencing the prescribing patterns and the behavior of health care professionals. The principal mechanisms used are formularies and reimbursement levels.

PBMs and similar service providers administer pharmacy benefit services on behalf of health plan sponsors, including managed care organizations, self-insured employers, insurers, unions, Medicaid and Medicare managed care plans, the Federal Employees Health Benefits Program, and other federal, state, and local government entities.[240] A principal method PBMs may use to control drug costs is drug formularies (described above supra part 4.d.3). A formulary influences the use of certain drugs over others in the same therapeutic class, and the mix of drugs dispensed overall, by restricting to some degree or completely the ability of a physician to prescribe a particular drug, or the ability of a patient to receive reimbursement for his or her purchase if prescribed. Drug formularies may be open, closed, or incentive-based.[241] With open formularies, a payor generally covers all drugs except those specifically

238. *See* Compliance Program Guidance for Pharm. Mfrs., 68 Fed. Reg. 23,731, 23,731 (May 5, 2003).
239. 21 U.S.C. §§ 801-830 (setting forth the Controlled Substances Act).
240. *See* A DOSE OF COMPETITION, ch. VII, *supra* note 203, at 10-18.
241. FDA PROFILE, *supra* note 181, § 2.2.

excluded. In closed formularies, a payor will list covered drugs, requiring plan enrollees to pay full cost for those not listed in the formulary.[242] Incentive-based formularies have lower copays for preferred formulary drugs.[243] These formularies may include tiered arrangements, in which the lowest copays are for generic products. Preferred brand name drugs having no generic alternatives would be on the next lowest copay tier. Nonpreferred brand name drugs would have the highest copays.

Although the inclusion of a product on the PBM formulary can result in a significantly reduced price to the plan participant as the ultimate purchaser for that product, the structure of the formulary also can play a significant role in the plan participant's choice of treatment or the accessibility of a given treatment at all, by excluding particular products from reimbursement or imposing copays that render use of the drug by plan enrollees economically impractical.

To position their products favorably for coverage and reimbursement by third-party payment plans, pharmaceutical manufacturers offer rebates to PBMs, in the form of either a formulary or market share payments.[244] Formulary payments are used by drug manufacturers to obtain formulary status from PBMs and health care plans and favorable placement within any tiers.[245] Market share payments, based on a drug's market share of that therapeutic class of drugs for plan members, are used by drug manufacturers to encourage PBMs to dispense a manufacturer's drug product, particularly when multiple products are approved within a therapeutic class.[246]

Manufacturers may also seek to promote the superiority of their products by providing various types of studies to the committees established by PBMs to design drug formularies. In developing a formulary, PBMs typically use an independent pharmacy and therapeutics (P&T) committee of physicians and pharmacists to evaluate

242. *Id.*
243. *Id.*
244. FTC, PBMs: OWNERSHIP OF MAIL-ORDER PHARMACIES, *supra* note 65, ch. 1, at 7.
245. *Id.*
246. *Id.*

drugs in different therapeutic classes.[247] Such committees usually consider a number of factors when deciding on coverage or placement of a particular drug in the formulary, including the drug's clinical safety and efficacy, market share, pricing, and the availability of generic and therapeutic alternatives.

For brand name drugs, PBMs historically have paid to the pharmacy a negotiated amount calculated as a discount from the AWP as stated by the manufacturer. The AWP reference price system has now been replaced, by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, with a new reference price, the ASP. For generic drugs, the MAC, as specified by the PBM, is used as the amount to which the discount is applied. Additionally, some agreements between the manufacturer and the PBM may allow for a rebate based on a percentage of ASP, or the achievement by the PBM of a specific share or sales target for the particular drug. Similarly, some agreements provide for payments by the drug manufacturers to the PBM for the preferred placement of certain products on the PBMs formulary.

2. *Generic Competition*

In contrast to brand name pharmaceutical companies, generic manufacturers compete primarily based on price. PBMs negotiate with manufacturers of generics concerning formulary placement. In addition, wholesalers negotiate with generics manufacturers to obtain favorable prices. Generics manufacturers do not undertake advertising or promotion for their drugs, since the uses and benefits of the drugs have been promoted previously by the brand name manufacturers to prescribers.

Generic manufacturers additionally compete to obtain the 180-day exclusivity period under the Hatch-Waxman Amendments that is accorded to the first generic manufacturer to file a complete Abbreviated New Drug Application (ANDA) for approval by the FDA with a Paragraph IV certification regarding patent status.[248] The Hatch-

247. *Id.* at 10.
248. 21 U.S.C. § 355(j)(5)(B)(iv). A discussion of the Hatch-Waxman Amendments can be found at Chapter II.B.

Waxman Amendments prohibit generic manufacturers whose ANDAs are approved by the FDA subsequent to the first filer from marketing their products until expiration of the initial exclusivity period. The exclusivity period provides an important incentive for filing prompt and complete ANDAs: generally, the first generic drug approved is priced 15 percent to 20 percent below the brand version; but when the 180-day exclusivity period expires and additional generic versions become available, prices generally fall to as much as 80 percent to 90 percent below the brand name drug's price level prior to introduction of any generic.[249] Some brand name manufacturers have opted to introduce generic versions of their brand products prior to expiration of their remaining exclusivity periods, termed "authorized generics," in order to obtain some share of generic sales of the product. Such authorized generics are not prohibited from being marketed during the 180-day exclusivity period for the first approved ANDA.

Generic drug competition currently is potentially available only for conventional (small-molecule) drugs, because the ANDA provisions of the Hatch-Waxman Act apply only to brand name drugs for which New Drug Applications (NDAs) have been approved.[250] As discussed at Chapter II(A)(1)(b), biologic products, by contrast, are approved through Biologics License Applications (BLAs) under the Public Health Service Act.[251] That law includes no regulatory pathway to approve follow-on generic biologics or "biosimilars," as exists in the European Union, to address cost concerns for such products.

Both state and private health care insurance programs have sought to encourage generic drug use to reduce health care costs.[252] Many third-

249. *See supra* discussion accompanying notes 28-31.
250. 42 U.S.C. §§ 262-263.
251. *Id.*
252. The only generic biologic product so far approved by FDA, a human growth hormone, is an anomaly; although a biologic, the applicable products were approved under NDAs and thus are subject to ANDAs under the Hatch-Waxman Amendments. The agency's approval came after a court order obtained by the generic manufacturer directing FDA to make a decision on the generic's section 505(b)(2) application, which the agency had held in abeyance pending consideration of scientific issues. *See* Sandoz Inc. v. Leavitt, [Transfer Binder Decisions 2006-2007] Food, Drug, Cosm. L. Rep. (CCH) ¶ 38,870 (D.D.C. 2006).
253. *Opportunities to Achieve Substantial Savings for Patients Through Greater Generic Pharmaceutical Utilization: Hearing Before the H. Energy and Commerce Subcomm. on Health* (2005) [hereinafter Jaeger Testimony] (statement of Kathleen Jaeger, GPhA President & CEO).
254. DEP'T OF HEALTH & HUMAN SERVS., CTRS. FOR MEDICARE & MEDICAID SERVS., SAFE AND EFFECTIVE APPROACHES TO LOWERING STATE PRESCRIPTION DRUG COSTS: BEST PRACTICES AMONG STATE MEDICAID DRUG PROGRAMS (SEPT. 9, 2004), *available at* http://www.cms.hhs.gov/MedicaidDrugRebateProgram/downloads/StateStrategiestoLowerMedicaidPharmacyCosts.pdf.
255. FTC PHARM. INDUS. REPORT, *supra* note 196, at 18.

party payors, including Medicaid, for example, require generic substitution unless the physician has indicated that the brand name drug should be dispensed. These programs instruct how prescribers may override the generic default. Some permit the physician to check a box or sign on a separate line for "Brand only" or "Dispense as written," or to write out such information on the prescription in the absence of a check box or signature line.[253] Other programs require a prior authorization for a brand name drug if generic alternatives exist, or require that the patient try and then fail to tolerate or improve with use of generic products before the brand name version may be dispensed.[254]

In addition to using their health care programs to further generic use, many states also promote generic use through laws permitting pharmacists to substitute generics, unless the prescriber has indicated brand only or dispense as written.[255] Some states have taken this even further by mandating generic substitution, unless the physician indicates otherwise.

Because FDA-approved generic drugs may differ in bioavailability[256] from their brand name counterparts (up to +/- 20%),[257] mandatory generic substitution programs often contain "carve-outs" for classes of drugs believed to have narrow therapeutic ranges, such as mental health, epileptic, and cancer drugs.[258] However, in an effort to reduce prescription drug costs further, many generic substitution programs are eliminating such exemptions.[259] Questions remain, however, as to whether generic substitution is medically appropriate for certain drugs.[260]

Other methods used by both third-party private payors and states to increase generic use include providing higher dispensing fees for pharmacists when generics are dispensed,[261] and sponsoring educational programs to patients and providers to promote generic alternatives. These efforts focus on raising awareness of generic alternatives and emphasize the sameness and low costs of generic alternatives.[262]

256. The FDA has defined the term "bioavailability" to mean "the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of action." 21 CFR § 320.1(a).
257. FOOD & DRUG ADMIN., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, at vi-viii (27th ed. 2007) (also known as the "*Orange Book*"). *See infra* Chapter II.A.2 (discussing FDA requirements for generic drugs).
258. Jaeger Testimony, *supra* note 253.
259. *Id.*
260. *See, e.g.*, Jacki Gordon & Steven C. Schachter, Generic and Brand Name AEDs—Considerations for Clinicians and Patients (Oct. 26, 2006), http://professionals.epilepsy.com/page/generic_considerations.html (discussing reports of increased breakthrough seizures in patients when switched from a brand name to a generic antiepileptic drug).
261. Jaeger Testimony, *supra* note 253.
262. *See, e.g.*, Generic Pharm. Ass'n, State Consumer Education Efforts, http://www.gphaonline.org/issues/state-consumer-education-efforts.

3. *Over-the-Counter Drugs*

Competition for OTC drug products is significantly different from that for prescription drugs. OTC products are purchased directly by consumers, without the requirement of a prescription, and are generally not covered by third-party insurance. As a result, price is a significant factor. Innovation is much less of a competitive factor because of the significantly different FDA regulatory approval pathway for these products. Unlike prescription drugs, OTC products are not subject to specific product approval procedures; rather, they may use only certain active pharmaceutical ingredients (APIs) with certain types of indications (claims) authorized by FDA. FDA has evaluated these APIs and created OTC monographs or proposed monographs for specific therapeutic classes. The monographs specify the conditions under which the ingredients listed in the monographs are GRAS/E[263] for specific OTC indications. New ingredients, not previously included in a monograph, such as those used in foreign markets, can be proposed for inclusion.

A small number of drugs have been approved for OTC use through FDA's NDA approval process. This may be done in two ways: If a product is first approved by FDA as a prescription product pursuant to a traditional NDA, a drug manufacturer may file a supplemental NDA with data and information to support the safe marketing of the drug as an OTC product. If FDA determines that the product can be used safely and effectively without physician assistance, the product may then be switched to OTC status. A drug manufacturer also may file a new NDA for OTC use, containing clinical trial data supporting safety and efficacy for OTC indications.

263. To be GRAS/E the product must be recognized among qualified scientific experts to be safe and effective for use under the indicated conditions, based on adequate published data (generally, rising to the same level of evidence that would be required for approval of a new drug application), and the drug must have been in use for the given indication for a material length of time. 21 U.S.C. § 321(p)(1)-(2).

a. Advertising and Promotion

Unlike prescription products, OTC products may be purchased by patients without a physician intermediary. Most advertising and promotion for OTC products thus is directed toward consumers, rather than to health care professionals. While prescription drug advertising is regulated by FDA, OTC drug advertising and promotion generally is monitored by the FTC, under its advertising substantiation standards. Because OTC products in a particular therapeutic class all must use the same approved APIs, and there are no clinical trial testing requirements as with prescription products; competition is focused on consumer brand name awareness and on time extensions (e.g., different dosage formulations and delivery types, such as gel caps, tablets, timed-released doses). Price competition among brand products also is prevalent, including standard consumer promotional activities, such as price discounting through coupons.

b. Generic Competition–Store Brands

Because FDA approves APIs by therapeutic classes for OTC products, rather than (as with prescription drugs) approving particular OTC products, barriers to entry are very low for store brand (that is, generic or private label) OTC products. Most retailers thus offer a store brand version of the more common or popular OTC products, attracting purchasers predominately by offering prices lower than those of the comparable brand name product. In addition, placement or display of OTC products bearing the store brands adjacent to name brands, and packaging highlighting the similarities of the active ingredients, play a significant competitive role. Store pharmacists may also direct consumers to consider store brand OTC products when consumers seek pharmacists' advice.

CHAPTER II

REGULATORY AND ENFORCEMENT FRAMEWORK

All pharmaceutical products are regulated by the FDA. No new drug or biologic can be marketed lawfully in the United States without authorization by the FDA. Authorization signifies that the new drug or biologic is safe and effective for its intended uses.

A. FDA Drug Approval Requirements

1. Innovative Drugs

a. Drugs (Small Molecules)

The FDCA,[1] as amended, regulates drug manufacturing, marketing, and distribution.[2] The FDCA grants the FDA, as the designee of the Secretary of HHS, the authority to regulate, among other items, drugs and devices.[3] The Act defines the term drug to include "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and "articles (other than food) intended to affect the structure or any function of the body."[4] Whether an article is a drug for purposes of the Act, therefore, often turns on the intended uses of the article.[5]

How a product is advertised and sold may make it a drug. Drugs include more than just medicines: fluoride toothpastes, antiperspirants, dandruff shampoos, and sunscreens are all considered drugs. In fact, the definition of drug is "broader than any strict medical definition might otherwise allow."[6]

The FDCA further grants the FDA the authority to regulate so-called combination products, which "constitute a combination of a drug, device,

1. 21 U.S.C. §§ 301-397.
2. Thompson v. W. States Med. Ctr., 535 U.S. 357, 361 (2002).
3. 21 U.S.C. §§ 321(g)-(h), 393.
4. *Id.* § 321(g)(1)(C).
5. United States v. Livdahl, 459 F. Supp. 2d 1255, 1259 (S.D. Fla. 2005).
6. United States v. Article of Drug Bacto-Unidisk, 394 U.S. 784, 798 (1969).

challenge, brought under a Sherman Act section 2[338] monopoly leveraging theory by purchasers against a research pharmaceutical company for its practice of pricing its AIDS drug, when used alone, at a higher price than when used as part of an AIDS "cocktail" of drugs, was rejected by one court on the basis that only one monopoly profit could be obtained by the manufacturers.[339] By contrast, another court held the same conduct could violate Sherman Act Section 2.[340]

Differential pricing among different customers by pharmaceutical manufacturers also has been challenged by retail pharmacies as price discrimination in violation of the Robinson-Patman Act.[341] The act prohibits price differentials of goods of like grade and quality sold reasonably contemporaneously to competing resellers, where the effect is substantially to lessen or injure competition.[342] The federal courts have not squarely addressed price discrimination in the context of managed care discounting by manufacturers. In a recent decision of the Federal District Court for the Eastern District of New York, however, the court granted partial summary judgment in favor of two manufacturers, Searle and Novartis.[343] In a wide-ranging discussion of the essential elements of a Robinson-Patman Act claim, the court ruled that the plaintiffs were unable to show a triable issue on the question of damages and that plaintiffs had failed to show that any sale had taken place when HMOs received manufacturer rebates but did not take title to the product. The court did find, however, that there were triable fact issues concerning competition between HMOs and retailers.

338. 15 U.S.C. § 2.
339. *See* Schor v. Abbott Labs., 457 F.3d 608 (7th Cir. 2006).
340. *See* Meijer, Inc. v. Abbott Labs., 544 F. Supp. 2d 995 (N.D. Cal. 2008).
341. 15 U.S.C. § 13a.
342. There are exemptions from the Robinson-Patman Act, including for sales to nonprofit institutions, such as charitable hospitals. *See* 15 U.S.C. § 13c.
343. *See* Drug Mart Pharm. Corp. v. Am. Home Prods. Corp., 472 F. Supp. 2d 385 (E.D.N.Y. 2007).

CHAPTER III

ASSESSING MARKET POWER

A. Market Power, Monopoly Power, and Market Definition

Antitrust law is principally concerned with conduct that poses a sufficient threat to competition and consumer welfare. Absent some material degree of market power, firms cannot adversely affect the competitive process.[1] Thus, before unilateral conduct, concerted action, or a proposed merger can be condemned under antitrust law, the relevant firms must be shown to possess sufficient market power such that their conduct might harm competition.

The standard for defining market power may differ depending on the violation alleged. For cases alleging unlawful agreements under Section 1 of the Sherman Act, other than those to which the per se rule applies, the market power requirement is generally defined as "the ability to raise prices above those that would be charged in a competitive market."[2] A similar standard applies in determining under Section 7 of the Clayton Act whether a merger will "create or enhance market power or . . . facilitate its exercise."[3]

For cases alleging unlawful monopolization or attempted monopolization under Section 2 of the Sherman Act, the courts require "monopoly power," which is "something greater than market power

1. *See generally* 1 JOHN MILES, HEALTH CARE AND ANTITRUST LAW § 5:3 (2008).
2. NCAA v. Bd. of Regents, 468 U.S. 85, 109 n.38 (1984); *accord* Jefferson Parish Hosp. Dist. No. 2 v. Hyde, 466 U.S. 2, 27 n.46 (1984) ("market power exists whenever prices can be raised above the levels that would be charged in a competitive market"). Section 1 cases, which involve conduct, such as price fixing, condemned under per se standards "are so plainly anticompetitive that no elaborate study of the industry is needed to establish their illegality." Nat'l Soc'y of Prof'l Eng'rs v. United States, 435 U.S. 679, 692 (1978).
3. U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, HORIZONTAL MERGER GUIDELINES § 0.1 (1992) (with Apr. 8, 1997 revisions) [hereinafter HORIZONTAL MERGER GUIDELINES] (market power generally refers to "the ability profitably to maintain prices above competitive levels for a significant period of time."), *available at* http://www.usdoj.gov/atr/public/guidelines/horiz_book/hmg1.html.

under § 1."[4] A typical formulation of the enhanced requirement for Section 2 defines monopoly power as "the power to charge a price higher than the competitive price without inducing so rapid and great an expansion of output from competing firms as to make the supracompetitive price untenable."[5]

The analysis of monopoly power and market definition is also context-sensitive. "[T]he nature of the claim can affect the proper market definition."[6] As the First Circuit noted in *U.S. Healthcare v. Healthsource, Inc.*,[7] "rational treatment is assisted by remembering to ask, in defining the market, *why* we are doing so: that is, what is the antitrust question in this case that market definition aims to answer?"[8]

The prescription drug industry has special characteristics that play an important role in the analysis of market power. The interplay between federal regulation, a unique patent protection scheme, and the control over purchasing decisions exercised by physicians and third-party payors complicates the analysis of market power for these products.

The following discussion focuses on two broad categories in which the approach to market power is a critical issue: anticompetitive conduct (part B) and mergers (part C). In each context, the market definition in assessing market power has become less certain and federal enforcement

4. Reazin v. Blue Cross & Blue Shield of Kan., Inc., 899 F.2d 951, 966 (10th Cir. 1990) (defining monopoly power as "substantial market power"); Deauville Corp. v. Federated Dep't Stores, 756 F.2d 1183, 1192 n.6 (5th Cir 1985) (defining monopoly power as an "extreme degree of market power").
5. *In re* Lorazepam & Clorazepate Antitrust Litig., 467 F. Supp. 2d 74, 86 (D.D.C. 2006) ("A firm is generally considered to have monopoly power if it can profitably raise prices substantially above the competitive level for a non-transitory period of time."); Harrison Aire, Inc. v. Aerostar Int'l, 423 F.3d 374, 380 (3d Cir. 2005) (citation omitted); United States v. Microsoft Corp., 253 F.3d 34, 51 (D.C. Cir. 2001) (en banc) (per curiam) ("[A] firm is a monopolist if it can profitably raise prices substantially above the competitive level.").
6. U.S. Healthcare v. Healthsource, Inc., 986 F.2d 589, 598 (1st Cir. 1993).
7. *Id.*
8. *Id.*

agencies have increasingly blended market definition with competitive effects.

B. Market Power in Conduct Cases

1. Traditional Market Definition

The market definition method of assessing market power relies on an economic inference that a high share of a properly defined relevant market, when combined with other market conditions—such as barriers to entry or expansion or high switching costs—reflects market power and thus the ability to price above the competitive level.[9] The first steps in this method require defining the relevant antitrust market and then determining the market share of an allegedly dominant firm (or combination of firms).

The relevant market for antitrust purposes has two dimensions: geographic and product. A geographic market is defined to be the "region such that a hypothetical monopolist that was the only present or future producer of the relevant product at locations in that region would profitably impose at least a 'small but significant and nontransitory' increase in price.'"[10] The competition arena for pharmaceutical products is national in scope, and federal regulations create significant barriers to

9. *See* Allen-Myland v. IBM Corp., 33 F.3d 194, 209 (3d Cir. 1994) ("'Market share [in a relevant market] is just a way of estimating market power, which is the ultimate consideration. When there are better ways to estimate market power the court should use them.'") (citation omitted)); Weiss v. York Hosp., 745 F.2d 786, 826 (3d Cir. 1984) ("[T]he purpose of market definition is to determine whether market power exists.").
10. HORIZONTAL MERGER GUIDELINES, *supra* note 3, § 1.21; *see also* Heerwagen v. Clear Channel Commc'ns, 435 F.3d 219, 228 (2d Cir. 2006) ("The relevant geographic market for antitrust purposes is some geographic area in which a firm can increase its price without 1) large numbers of customers quickly turning to alternative supply sources outside the area; or 2) producers outside the area quickly flooding the area with substitute products," *quoting* HERBERT HOVENKAMP, FEDERAL ANTITRUST POLICY: THE LAW OF COMPETITION AND ITS PRACTICE § 3.6 at 113 (2d ed. 1999)).

the entry of foreign drugs into the United States.[11] Because of these factors, the relevant geographic market (for U.S. antitrust purposes) for pharmaceuticals is typically the entire United States and is seldom contested. The battle over the relevant market therefore centers on product market definition.

The idea underlying the traditional approach is that the existence of one or more close economic substitutes for a product will constrain the ability of the firm selling that product to exercise market power—i.e., to raise or maintain prices above the competitive level, reduce output, or otherwise engage in efforts to reduce competition.[12] The principal issue is whether existing competitors or potential entrants can prevent an incumbent firm from charging prices above competitive levels or engaging in other anticompetitive conduct.[13] Where an incumbent product faces close economic substitutes, those substitutes will create competitive pressure on prices or other forms of competitive activity.[14] Those substitutes, then, belong in an appropriately defined relevant market. If other products do not exert sufficient competitive pressure on a rival, those products do not belong in the relevant market.[15] "The outer

11. For a discussion of FDA regulations, see *supra* Chapter II.
12. United States v. Microsoft Corp., 253 F.3d 34, 57 (D.C. Cir. 2001) (en banc) (per curiam) ("Structural market power analyses are meant to determine whether potential substitutes constrain a firm's ability to raise prices above the competitive level . . . .").
13. 2A PHILLIP E. AREEDA & HERBERT HOVENKAMP ET AL., ANTITRUST LAW: AN ANALYSIS OF ANTITRUST PRINCIPLES AND THEIR APPLICATION ¶¶ 533, 536 (2d ed. 1995).
14. *See, e.g.*, Elizabeth Mensch & Alan Freeman, *Frontiers of Legal Thought: Efficiency and Image: Advertising as an Antitrust Issue*, DUKE L.J. 321, n.135 (1990) ("Perhaps the most important technique of nonprice competition is advertising.").
15. Geneva Pharms. Tech. Corp. v. Barr Labs., 386 F.3d 485, 496 (2d Cir. 2004) ("The goal in defining the relevant market is to identify the market participants and competitive pressures that restrain an individual firm's ability to raise prices or restrict output. The relevant market is defined as all products 'reasonably interchangeable by consumers for the same purposes,' because the ability of consumers to switch to a substitute restrains a firm's ability to raise prices above the competitive level." (citation omitted)); *Microsoft*, 253 F.3d at 51 ("[A] firm is a monopolist if it can profitably raise prices substantially above the competitive level.").
16. Brown Shoe Co. v. United States, 370 U.S. 294, 325 (1962); *see also* Queen City Pizza v. Domino's Pizza, 124 F.3d 430, 436 (3d Cir. 1997).
17. *Microsoft*, 253 F.3d at 53–54.
18. *See, e.g.*, Telecor Commc'ns v. S.W. Bell Tel., 305 F.3d 1124, 1132 (10th Cir. 2002) ("Reasonable interchangeability does not depend on product similarity."); U.S. Anchor Mfg. v. Rule Indus., 7 F.3d 986, 995-99 (11th Cir. 1993) (finding, despite functional interchangeability, absence of price-related demand and supply elasticities prevents products from residing in same market); United States v. Archer-Daniels-Midland Co., 866 F.2d 242, 248 & n.1 (8th Cir. 1988) (finding that sugar and high fructose corn syrup, though functionally interchangeable, do not reside in the same antitrust product market because "a small change in the price of HFCS would have little or no effect on the demand for sugar" such that cross-elasticity of demand is low, despite evidence of actual substitution of corn syrup for sugar by consumers).

boundaries of a product market are therefore determined by the reasonable interchangeability of use or the cross-elasticity of demand between the product itself and substitutes for it."[16] A relevant market includes "only substitutes that constrain pricing in the reasonably foreseeable future."[17]

Mere functional substitutability is not enough to define a relevant product market.[18] To be reasonably interchangeable for product market definition purposes, products must be both (1) functionally

interchangeable, and (2) economically substitutable.[19] As one court noted:

> [A]lmost all products have substitutes: even buses, skywriters and road signs compete with newspapers for advertising. Antitrust law, however, is only concerned with products reasonably interchangeable with one another, in other words, products for which there is some cross elasticity of demand.[20]

Cross-price elasticity of demand reflects the degree to which products are "economic substitutes," i.e., whether the relative change in the price of one product causes commensurate shifts in sales to, or from, the other. In *Brown Shoe Co. v. United States*,[21] the Supreme Court identified a

19. As the Ninth Circuit has explained:
> Where an increase in the price of one product leads to an increase in demand for another, both products should be included in the relevant product market. The determination of what constitutes the relevant product market hinges, therefore, on a determination of those products to which consumers will turn, given reasonable variations in price.

Lucas Auto. Eng'g v. Bridgestone/Firestone, 275 F.3d 762, 767 (9th Cir. 2001) (citation omitted); *see also U.S. Anchor Mfg.*, 7 F.3d at 995-99; Hayden Publ'g v. Cox Broad., 730 F.2d 64, 70-71 (2d Cir. 1984); SmithKline Corp. v. Eli Lilly & Co., 575 F.2d 1056, 1064-65 (3d Cir. 1978); Pinder v. Hudgins Fish Co., 570 F.2d 1209, 1220 n.17 (5th Cir. 1978).

20. Auburn News v. Providence Journal Co., 504 F. Supp. 292, 302 (D.R.I. 1980) (*citing Brown Shoe*, 370 U.S. at 294), *rev'd on other grounds*, 659 F.2d 273 (1st Cir. 1981). In addition, the degree of cross-elasticity of demand must be significant. *See, e.g.*, Forsyth v. Humana, Inc., 114 F.3d 1467, 1483 (9th Cir. 1997) (Wallace, J., concurring and dissenting) ("A high cross elasticity of demand indicates that products are close substitutes, and should probably be treated as part of the same market. A low or zero cross elasticity of demand is evidence that products do not compete in the same relevant market."); Fed. Trade Comm'n v. Staples, Inc., 970 F. Supp. 1066, 1078 (D.D.C. 1997) (stating that low cross-elasticity results in exclusion of products in antitrust market).

21. 370 U.S. 294 (1962).

variety of factors that can be considered as part of that analysis, including: industry or public recognition of a distinct market, a product's peculiar characteristics and uses, unique production facilities, distinct customers, distinct prices, sensitivity to price changes, and specialized vendors.[22] These factors help to establish the "outer boundaries of a product market,"[23] but are themselves mere proxies for assessing the cross-elasticity of demand between products alleged to be in the same market.[24] The *Brown Shoe* factors are "meant as practical aids," and "their presence or absence" will not "dispose, in talismanic fashion" of the issue of defining of the relevant product market.[25]

In many industries, if products are, to some degree, "functionally interchangeable" for their intended purpose, such products will theoretically constrain each seller's ability to raise price above

22. *Id.*

23. *Id.*

24. As the Eleventh Circuit has observed:
> Reliable measures of supply and demand elasticities provide the most accurate estimates of relevant markets. However, it is ordinarily quite difficult to measure cross-elasticities of supply and demand accurately . . . . Therefore, it is usually necessary to consider other factors that can serve as useful surrogates for cross-elasticity data . . . . In the case of product market definition, these factors may include whether the products and services have sufficiently distinctive uses and characteristics; whether industry firms routinely monitor each other's actions and calculate and adjust their own prices (at least in part) on the basis of other firms' prices; the extent to which consumers consider various categories of sellers . . . as substitutes; and whether a sizeable price disparity between different types of . . . sellers . . . persists over time for equivalent amounts of comparable goods and services."

U.S. Anchor Mfg. v. Rule Indus., 7 F.3d 986, 995 (11th Cir. 1993) (omissions in original) (citations omitted); *see also* Rothery Storage & Van Co. v. Atlas Van Lines, 792 F.2d 210, 218-19 n.4 (D.C. Cir. 1986) (explaining how *Brown Shoe* factors relate to cross-elasticity of demand); HORIZONTAL MERGER GUIDELINES, *supra* note 3, § 1.0 (defining market).

25. *Staples, Inc.*, 970 F. Supp. at 1075; *see also Rothery*, 792 F.2d at 218-19 n.4.

competitive levels.[26] However, certain aspects of the pharmaceutical industry can significantly disconnect functional or therapeutic interchangeability from economic substitutability.[27]

a. Competition Among Branded Products

When the issue is conduct that allegedly affects competition between branded pharmaceutical products, the distinctive characteristics of competition between branded drugs becomes important to the issue of market definition and market power. As described earlier,[28] competition between branded drugs tends to focus *not* on price, but rather on innovation (research and development of new indications and uses for the branded product) and marketing (communicating the results of research and development efforts to doctors and patients).[29] Such

26. *See, e.g.*, U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, COMMENTARY ON THE HORIZONTAL MERGER GUIDELINES 6 (2006) [hereinafter COMMENTARY ON THE HORIZONTAL MERGER GUIDELINES]:

> Defining markets under the Guidelines' method does not necessarily result in markets that include the full range of functional substitutes from which customers choose. That is because, as the Guidelines provide, a "relevant market is a group of products and a geographic area that is no bigger than necessary to satisfy [the hypothetical monopolist] test."

HORIZONTAL MERGER GUIDELINES § 1.0. This is one of several points at which the Guidelines articulate what is referred to in Section 1.21 as the "'smallest market' principle" for determining the relevant market. The Agencies frequently conclude that a relatively narrow range of products or geographic space within a larger group describes the competitive arena within which significant anticompetitive effects are possible.

27. *See In re* Cardizem CD Antitrust Litig., 200 F.R.D. 297, 311 (E.D. Mich. 2001) ("[T]he pharmaceutical market is fundamentally different from the market for other products.").
28. *See supra* Chapter I.C.1.
29. *See* CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 21 (1998) [hereinafter CONG. BUDGET OFFICE], *available at* http://www.cbo.gov/ftpdocs/6xx/doc655/pharm.pdf; Mark A. Hurwitz & Richard E. Caves, *Persuasion or Information? Promotion and the Share of Brand-Name and Generic Pharmaceuticals*, 31 J.L. & ECON. 299, 302 (1988).

competition affects the brand name drug's perceived value, but has a reduced effect on price competition.[30] Prescribing physicians are also generally insensitive to drug prices[31] because they select medicines based on other criteria, namely the effect the drug will have on the health and well-being of their patients. Thus, the mere fact of substitutability between brand drugs within a therapeutic class does not necessarily suggest price constraint among branded products.[32]

This is not to say that price competition never exists between branded products or that physicians never take price into account when choosing among brands within a particular therapeutic class. Prior to generic entry, the presence of other brand name products (as well as non-AB-rated generic drugs, i.e., generics corresponding to other brands) in the same therapeutic class can restrain brand pricing. The intense public

30. Promotional efforts by branded manufacturers also tend to decrease price sensitivity. John A. Rizzo, *Advertising and Competition in the Ethical Pharmaceutical Industry: The Case of Antihypertensive Drugs*, 42 J.L. & ECON. 89, 107, 112-13 (1999); *see* Henry Grabowski & John Vernon, *Longer Patent for Increased Generic Competition in the U.S.: The Waxman-Hatch Act After One Decade*, 10 PHARMACOECONOMICS 110, 111-18 (Supp. No. 2 1996); NAT'L INST. FOR HEALTH CARE MGMT., CHANGING PATTERNS OF PHARMACEUTICAL INNOVATION 3 (2002) ("This pattern suggests that when there are several new NMEs [(New Molecular Entities)] in a therapeutic class, price competition among them is limited . . . ."), *available at* http://nihcm.org/~nihcmor/pdf/innovations.pdf.
31. *See, e.g.*, SmithKline Corp. v. Eli Lilly & Co., 575 F.2d 1056, 1063 (3d Cir. 1978) ("Prescribing physicians are not cost conscious in their choices of an antibiotic for a hospitalized patient, and so do not opt for a less expensive over a more costly medication."). *But see, e.g.*, M. Howard Morse, *Product Market Definition in the Pharmaceutical Industry*, 71 ANTITRUST L.J. 633, 663 (2003) (noting some physicians may factor price into their selection).
32. *Cf. SmithKline*, 575 F.2d at 1063-64 (holding that two drug molecules that could be used for the same purpose were not part of the same market because cross-price elasticity between the two was absent).

concern with, and scrutiny of, medical costs,[33] particularly prescription pharmaceutical costs, also creates a variety of pressures on prices.[34] Moreover, as the FTC's merger enforcement decisions signify,[35] nonprice competition is an important dimension of rivalry which can also center product market definition. All of these factors will influence a market definition analysis in a case involving competitive effects in a marketplace consisting solely of branded drugs.

b. Competition From Generic Products

Where the conduct involves actual or potential competition between branded and generic drugs, the pricing dynamics change. As discussed below,[36] the entry of an AB-rated generic equivalent to the branded drug typically has a powerful effect on the market price for the drug molecule.[37] Customers frequently shift most of their business to generic suppliers within a short time, paying a fraction of the prices they formerly did for the same drug.[38] Indeed, upon generic entry, average prices may drop to 20 percent of the pre-generic entry level (or even lower).[39] At the same time, because the branded firm's efforts to build and maintain prescription volume ceases, and because generics typically

33. Sara Fisher Ellison & Catherine Wolfram, Pharmaceutical Prices and Political Activity 1-5 (2000), *available at* http://econ-www.mit.edu/files/990.
34. *See* Richard G. Frank & David S. Salkever, *Generic Entry and the Pricing for Pharmaceuticals*, 6 J. ECON. & MGMT. STRATEGY 75, 89 (1997).
35. *See infra* part C for a discussion of market power in merger cases.
36. *See supra* Chapter I.A.2.b for a discussion of the effect of generic entry on price.
37. The powerful effects of generic competition are described in the following sources: OFFICE OF TECH. ASSESSMENT, U.S. CONGRESS, PHARMACEUTICAL R&D: COSTS, RISKS, AND REWARDS 83-89, 243 (1993), *available at* http://www.fas.org/ota/reports/9336.pdf; CONG. BUDGET OFFICE, *supra* note 29, at ix, xii–xiii, 8–9, 13, 27–35; Duane M. Kirking, et al., *Economics and Structure of the Generic Pharmaceutical Industry*, 41 J. AM. PHARMACY ASS'N 578–84 (2001).
38. CONG. BUDGET OFFICE, *supra* note 29, at 27-29.
39. *Id.* at 32.

do little advertising or promotion, generic entry generally correlates with a plateau of growth, or sometimes even a unit sales volume decline in the specific drug molecule, despite the substantially lower average price.[40] For reasons discussed below,[41] this distinctive pricing dynamic complicates the analysis of market power and definition of the relevant market.

2. Direct Evidence

Although courts predominantly rely upon the relevant market analysis described above to determine the presence of market power, some courts evaluate market power by examining direct forms of proof, such as evidence of supracompetitive prices, profit margins, or effect on output.[42]

40. *Id.* Branded companies typically release a "next generation" version of the brand name drug undergoing generic competition, which can, and often does, have the effect of increasing total prescriptions in a therapeutic class, even if the number of prescriptions of the molecule facing direct generic competition falls.
41. *See infra* part B.3 for criticisms of the direct evidence approach.
42. Harrison Aire, Inc. v. Aerostar Int'l, 423 F.3d 374, 381 (3rd Cir. 2005) ("Monopoly power can be demonstrated with either direct evidence of supracompetitive pricing and high barriers to entry, or with structural evidence of a monopolized market." (citation omitted)); *see also* Dickson v. Microsoft Corp., 309 F.3d 193, 219 (4th Cir. 2002) (refusing to dismiss complaint alleging detrimental effects to competition; "While anticompetitive effect is often proven through analysis of the relevant market definition and market power, it can also be proven through actual anticompetitive effects"); Conwood Co. v. U.S. Tobacco Co., 290 F.3d 768, 783 (6th Cir. 2002) ("Whether a company has monopoly or market power 'may be proven directly by evidence of the control of prices or the exclusion of competition.'" (citation omitted)); United States v. Microsoft Corp., 253 F.3d 34, 51 (D.C. Cir. 2001) (if "evidence indicates that a firm has in fact [profitably raised prices substantially above the competitive level], the existence of monopoly power is clear"); Toys "R" Us, Inc. v. Fed. Trade Comm'n, 221 F.3d 928, 937 (7th Cir. 2000) (market power may be shown directly with proof of anticompetitive effects); Tops Mkts. v. Quality Mkts., 142 F.3d 90, 97-98 (2d Cir. 1998) (stating that market

The direct evidence approach has been advocated most strongly in cases alleging unlawful exclusion of generic competition. Proponents argue that determining whether a firm has obtained or is maintaining market power is not an end in itself. Rather, it is a means of determining whether the firm's conduct—unilateral or concerted—is likely to, or has in fact, resulted in artificially inflated excessive prices (or reduced output).[43] It should therefore not be necessary as an analytical matter to

power "may be proven directly by evidence of the control of prices"); Coastal Fuels of P.R. v. Caribbean Petroleum Corp., 79 F.3d 182, 196 (1st Cir. 1996) (market power exists when a firm "'(1) can profitably set prices well above its costs and (2) enjoys some protection against [a] rival's entry or expansion that would erode such supracompetitive prices and profits.'" (omission in original) (citation omitted)); Rebel Oil v. Atlantic Richfield Co., 51 F.3d 1421, 1434 (9th Cir. 1995) ("If the plaintiff puts forth evidence of restricted output and supracompetitive prices, that is direct proof of the injury to competition which a competitor with market power may inflict, and thus, of the actual exercise of market power"; substituting "restricted output" for "actual exclusion of competitors"); Flegel v. Christian Hosp., 4 F.3d 682, 688 (8th Cir. 1993) ("'Since the purpose of the inquiries into market definition and market power is to determine whether an arrangement has the potential for genuine adverse effects on competition, 'proof of actual detrimental effects, such as a reduction of output,' can obviate the need for an inquiry into market power, which is but a "surrogate for detrimental effects."'" (citation omitted)); Reazin v. Blue Cross & Blue Shield of Kan., Inc., 899 F.2d 951, 966-67 (10th Cir. 1990) ("'To demonstrate "market power," a plaintiff may show evidence of either "power to control prices" or "the power to exclude competition."' Market power is to be distinguished from monopoly power, which in this circuit requires proof of both power to control prices and power to exclude competition." (citation omitted)); Palmer v. BRG of Ga., Inc., 874 F.2d 1417, 1437 (11th Cir. 1989) ("[P]laintiffs can show actual detrimental effects, such as a reduction of output or increased price, instead of an inquiry into market power."), *rev'd on other grounds,* 498 U.S. 46 (1990).

43. *See* Todd v. Exxon Corp., 275 F.3d 191, 206 (2d Cir. 2001) ("If a plaintiff can show that a defendant's conduct exerted an actual adverse effect on competition, this is a strong indicator of market power. In fact, this arguably is more direct evidence of market power than calculations of elusive market share figures." (citation omitted)); Am. Floral Servs. v.

define a relevant market.[44] This would hold true whether the case implicates Section 1 or Section 2 of the Sherman Act.[45]

Florists' Transworld Delivery Ass'n, 633 F. Supp. 201, 221-22 (N.D. Ill. 1986) ("After all, market share is at best a proxy for market power, and a rough one at that. What really counts is the ability of a producer to control output and obtain 'supracompetitive prices.'" (citation omitted)). As one commentator recently observed:

> [I]f a firm or firms *successfully* engage in either collusionary or exclusionary conduct, the law presumes that it has or they have market power. Their success would be otherwise inexplicable. In that case, evidence of low market share is viewed as irrelevant at best, and at worst as a demonstrably unreliable index of that power. The burden then shifts to the defendant to defeat the evidence of market power—and to do so it must challenge the direct evidence; it cannot simply rely on contrary, circumstantial evidence in the form of low market shares.

Andrew I. Gavil, *Copperweld 2000: The Vanishing Gap Between Sections 1 and 2 of the Sherman Act*, 68 ANTITRUST L.J. 87, 99 (2000) (emphasis in original).

44. *See* Fed. Trade Comm'n v. Ind. Fed'n of Dentists, 476 U.S. 447, 460-61 (1986); *Toys "R" Us*, 221 F.3d at 937 ("TRU seems to think that anticompetitive effect in a market cannot be shown unless the plaintiff, or here the Commission, first proves that it has a large market share. This, however, has things backwards. As we have explained elsewhere, the share a firm has in a properly defined market is only a way of estimating market power, which is the ultimate consideration."); 2A AREEDA & HOVENKAMP ET AL., *supra* note 13, ¶ 531a ("Finding the relevant market and its structure is not a goal in itself but a surrogate for market power."); *id.* at ¶ 515 (resorting to "market-definition approach" is warranted when "no other observable facts establish the existence and degree of market power more directly").

45. As Professors Edlin and Rubinfeld recently observed: "Market definition is only a traditional means to the end of determining whether power over price exists. Power over price is what matters. . . . [I]f power can be shown directly, there is no need for market definition." Aaron Edlin & Daniel Rubinfeld, *Exclusion or Efficient Pricing? The 'Big Deal' Bundling of Academic Journals*, 72 ANTITRUST L.J. 119, 141 (2004) (citation omitted).

The pertinent inquiry under the direct proof approach—when examining either unilateral or allegedly collusive conduct—is therefore whether the conduct has permitted or would permit the firm or firms to raise or maintain prices above competitive levels. If one can prove that directly—for instance, by showing that after the alleged restraint of trade in question has ended, product price dropped substantially—indirect proof may become unnecessary. Direct evidence of market prices materially exceeding competitive levels for a substantial period of time may provide evidence that the restraint in question misallocates resources in an economic sense and reduces consumer welfare.[46]

3. Criticism of the Direct Evidence Method

The view that plaintiffs may rely on direct proof of allegedly supracompetitive pricing and profit margins to show market power or monopoly power, without the burden of proving a relevant market, is far from unanimous. With regard to Section 1 cases, one commentator has noted that "other than for conduct that is illegal per se without inquiry into actual effect, 'rule of reason' analysis . . . generally requires a detailed examination of a challenged agreement's effect in a well-defined market."[47] Regarding Section 2 claims of monopolization or attempted

46. Pool Water Prods. v. Olin Corp., 258 F.3d 1024, 1034 (9th Cir. 2001) (finding acts that harm allocative efficiency and raise the price of goods above the competitive level harm consumer welfare); *Rebel Oil*, 51 F.3d at 1433 (stating conduct harms consumer welfare "when it harms both allocative efficiency *and* raises the prices of goods above competitive levels or diminishes their quality"); Storer Cable Commc'ns v. City of Montgomery, 826 F. Supp. 1338, 1352 (M.D. Ala. 1993) ("eliminat[ing] or significantly diminish[ing] an important source of competitive pressure on price" has "a substantial adverse effect on consumer welfare").
47. *See* Morse, *supra* note 31, at 652 & n.70 (citing Copperweld Corp. v. Independence Tube Corp., 467 U.S. 752, 768 (1984) (rule of reason requires "an inquiry into market power and market structure designed to assess the combination's actual effect.")); *see also* Tanaka v. Univ. of S. Cal., 252 F.3d 1059, 1063 (9th Cir. 2001) ("A restraint violates the rule of reason if the restraint's harm to competition outweighs its procompetitive effects. The plaintiff bears the initial burden of showing that the restraint produces 'significant anticompetitive effects' within a 'relevant market.'") (citation omitted).

monopolization, the Supreme Court has held that "[w]ithout a definition of [the] market there is no way to measure [a defendant's] ability to lessen or destroy competition."[48]

There is also doubt about the reliability of using "standard accounting data used to report corporate profits" as an indicator of purported monopoly profits.[49] Firms' conventional accounting methods may not break costs down by product, complicating or possibly preventing the calculation of accurate profit margins.

In the pharmaceutical context, courts and commentators have questioned whether it is proper to rely solely on price and profit comparisons before and after generic entry in order to assess competitive effects.[50] They have argued instead that assessments of profits and costs should account for research and development costs, rather than only short run marginal costs (i.e., manufacturing costs).[51] Calls have also been made to account for nonprice competition, in the form of vigorous advertising and promotion and distribution of free samples, which tends to be the dominant mode of competition between different brand name drugs in the same therapeutic category.[52] Lastly, some have asserted that in analyzing pharmaceutical markets using the direct approach, the

48. Walker Process Equip. v. Food Mach. & Chem., 382 U.S. 172, 177 (1965); *see also In re* Remeron Direct Purchaser Antitrust Litig., 367 F. Supp. 2d 675, 680 n.7 (D.N.J. 2005); Morse, *supra* note 31, at 653-54.
49. Morse, *supra* note 31, at 671 & n.172. Indeed, in *Cipro*, the Court faulted plaintiffs for not introducing information regarding the costs to manufacture the drug. *In re* Ciprofloxacin Hydrochloride Antitrust Litig., 363 F. Supp. 2d 514, 523 (E.D.N.Y. 2005).
50. *See, e.g.*, Meijer, Inc. v. Barr Pharms., 572 F. Supp. 2d 38, 54-56 (D.D.C. 2008); *Remeron*, 367 F. Supp. 2d at 682-84; Morse, *supra* note 31, at 676 ("Plaintiffs in pharmaceutical cases cannot simply assume the existence of market power from the existence of patents, from pricing above short-run marginal cost, from generic entry at prices below the price of a branded drug, or from reduced output of the branded drug upon generic entry.").
51. *See, e.g.*, *Remeron*, 367 F. Supp. 2d at 682-83.
52. *See, e.g.*, *Meijer*, 572 F. Supp. 2d at 55.

proper focus should be on the impact of particular conduct on output, rather than prices.[53]

Research and development costs—Brand name drug manufacturers bear very large up-front costs for researching and developing new drugs.[54] In contrast, generic manufacturers avoid extensive research and development costs because they are permitted to rely on the brand drug's efficacy and safety studies in order to win FDA approval. Critics of the direct evidence approach argue that profit-margin comparisons that do not take these research and development costs into account are fundamentally flawed. For example, in *Remeron Direct Purchaser Antitrust Litigation*,[55] the court criticized the direct-evidence approach for failing to consider that the higher prices charged by brand companies

53. *See, e.g.*, Morse, *supra* note 31, at 676.

54. Published estimates of the costs to develop and bring a new drug to market (including, inter alia, the costs of all of those projects that do not result in a marketable product) range from approximately $200 million (CONG. BUDGET OFFICE, *supra* note 29, at 14-15) to $800 million. *See* Joseph A. DiMasi, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003). However, the latter number has been severely criticized. *See* MARCIA ANGELL, THE TRUTH ABOUT DRUG COMPANIES 42 (2004). For example, the figure is criticized as inflated because half the figure represents "opportunity costs of capital"; that is, hypothetical returns on investments were capital not spent on R&D. Also, the figure fails to recognize that much of the initial research for new chemical entities is performed by the National Institutes of Health or universities. Pharmaceutical companies also benefit from tax credits related to research and development. Lastly, the $800 million figure includes money spent on unrelated drugs (including failed drugs), rather than only a single chemical entity or product which might be at the core of an antitrust dispute. *See generally* PUBLIC CITIZEN'S CONGRESS WATCH, AMERICA'S OTHER DRUG PROBLEM: A BRIEFING BOOK ON THE RX DRUG DEBATE 46-55 (2002), *available at* http://www.citizen.org/documents/drugbriefingbk.pdf; Bette Hileman, *Accounting For R&D: Many Doubt The $800 Million Pharmaceutical Price Tag*, 84 CHEM. AND ENG'G. NEWS (No. 25) 50 (2006), *available at* http://pubs.acs.org/cen/pharma/8425bus_box2.html; MERRILL GOOZNER, THE $800 MILLION PILL: THE TRUTH BEHIND THE COST OF NEW DRUGS (2004).

55. 367 F. Supp. 2d 675 (D.N.J. 2005).

may simply "reflect a higher quality more costly to provide."[56] The court ruled that the plaintiffs' failure to adduce evidence of "an abnormally high price-cost margin" precluded a finding of monopoly power through allegedly supracompetitive pricing alone.[57]

Nonprice Competition—Another criticism of the direct proof approach is its perceived failure to account for the extent that branded pharmaceutical manufacturers compete in ways other than price. Such nonprice competition can include rivalry over research and development, and marketing and promotion.[58] Pharmaceutical firms expend considerable resources on research and development and, therefore, compete in development and introduction of new drugs.

Nonprice competition also may take the form of various techniques used to market drugs specifically to physicians, including detailing visits by pharmaceutical representatives to physicians' offices, handing out free samples, advertising in scientific journals, and educating physicians and the public on the benefits of the product. Each brand name company works to persuade physicians to prescribe its product over others within the same therapeutic category, often by portraying its product as different and better than other drugs, if not for all patients then at least for niche groups of patients.[59] Because advertising and promotion do not have unambiguous consumer benefits, however, market power (and market

56. *See id.* at 683 (citing Blue Cross & Blue Shield United v. Marshfield Clinic, 65 F.3d 1406, 1411-12 (7th Cir. 1995) ("when dealing with a heterogeneous product or service, such as the full range of medical care, a reasonable finder of fact cannot infer monopoly power just from higher prices—the difference may reflect a higher quality more costly to provide")); Harrison Aire, Inc. v. Aerostar Int'l, 423 F.3d 374, 381 (3rd Cir. 2005) ("a firm's high price may simply reflect a superior product").

57. *See In re* Remeron Direct Purchaser Antitrust Litig., 367 F. Supp. 2d 675, 682 (D.N.J. 2005); *see also* United States v. United Shoe Mach., 110 F. Supp. 295 (D. Mass. 1953) (factoring in research and development costs in determining whether monopoly power existed), *aff'd per curiam*, 347 U.S. 521 (1954).

58. *See* Morse, *supra* note 31, at 637-38.

59. *See* Rizzo, *supra* note 30, at 104-05.

definition) in antitrust cases has not typically been assessed based on nonprice factors.[60]

Restricted Output—Critics of the direct proof approach also argue that the critical measure of anticompetitive effect is restriction of output.[61] They further note that, despite the lower average prices that prevail after generic entry, output often stabilizes or falls for the molecule (brand plus generic volumes combined) following generic entry.[62] Facing imminent or actual generic competition, the brand name company typically ceases promotional efforts, discontinuing (or sharply limiting) all advertising, detailing, and educational efforts regarding its drug.[63]

Proponents of the direct evidence approach counter that any loss in output for the molecule must be weighed against the substantial savings in price from generic entry. They point out that a reduction in output is generally anticompetitive because it usually leads to an increase in price.[64] Here, reduced output is linked to (or coincident with) a dramatic

60. Richard J. Gilbert & Steven C. Sunshine, *Incorporating Dynamic Efficiency in Merger Analysis*, 63 ANTITRUST L.J. 569, 572 (1995) ("Antitrust analysis typically does not dwell on the nonprice aspects of competition. One reason is the difficulty of assessing consumer benefits from particular forms of nonprice competition. Other things being equal, consumers are unambiguously better off with lower prices. Whether consumers benefit from advertising and marketing expenditures, however, is unclear.").
61. *See, e.g.*, Geneva Pharms. Tech. Corp. v. Barr Labs., 386 F.3d 485, 500 (2d Cir. 2004) ("Nor do Plaintiffs show evidence that defendants restricted output."); *In re* Ciprofloxacin Hydrochloride Antitrust Litig., 363 F. Supp. 2d 514, 523 (E.D.N.Y. 2005) ("Plaintiffs have provided neither evidence of Bayer's costs nor any direct evidence that defendants restricted output.").
62. *See, e.g.*, Morse, *supra* note 31, at 675.
63. *See id.* (citing Richard G. Frank & David S. Salkever, *Generic Entry and the Pricing of Pharmaceuticals*, 6 J. ECON. & MGMT. STRATEGY 82 (1997)).
64. *See, e.g.*, *In re* Linerboard Antitrust Litig., 305 F.3d 145, 152 (3d Cir. 2002) ("A reduction in supply will cause prices to rise. A deliberate cut in supply, as alleged here, is a deliberate interference with market forces.").

drop in price. Hence, the reduced total output occasionally associated with generic entry may not be a meaningful anticompetitive effect (or is in any event less important than the obvious beneficial price effects of generic entry).

C. Market Power in Merger Cases

1. Market Definition and Direct Effects

The FTC has been the agency responsible for reviewing pharmaceutical mergers. It has analyzed pharmaceutical mergers in terms of their impact on actual competition, potential competition and innovation.[65] Under the agencies' *Horizontal Merger Guidelines*, the first step in the process is to define the relevant market.[66] As the agencies' methodology has evolved, however, the market definition exercise has been folded into the broader inquiry into likely competitive effects. Under the agencies' current approach:

> The market definition process is not isolated from the other analytic components in the Guidelines. The Agencies do not settle on a relevant market definition before proceeding to address other issues. Rather, market definition is part of the integrated process by which the Agencies apply Guidelines principles, iterated as new facts are learned, to reach an understanding of the merger's likely effect on competition.[67]

In some cases, the agencies may even start with competitive effects and work back to market definition.[68]

2. Product Markets

Brand name pharmaceuticals are grouped into categories known as therapeutic classes based on the medical indications for which drugs are

65. *See* Chapter IV for a discussion of competitive analysis in pharmaceutical mergers.
66. HORIZONTAL MERGER GUIDELINES, *supra* note 3, § 1.1.
67. COMMENTARY ON THE HORIZONTAL MERGER GUIDELINES, *supra* note 26, at 8.
68. *Id.* at 13.

approved—that is, what ailment they treat.[69] Drugs may then be sub-classified based on the mechanism of action or class of drug—that is, what chemical mechanism they use to interact with the body to treat an ailment.[70] For example, antidepressants constitute a therapeutic class. A sub-class based on its mechanism of action is "tricyclic agents," and one tricyclic agent is nortriptyline hydrochloride.[71] Drugs may then be further subdivided based on whether they have the same chemical compound as the active ingredient; whether they are available in a specific dosage form (i.e., tablet, capsule, liquid, topical, spray, or injectable); whether they have the same frequency of dosage; whether they have the same dosage strength; and whether they are being sold as a branded or generic version.[72]

Depending on the facts in any particular case, the FTC has factored each of these classifications into the definition of the relevant market.[73] For instance, in evaluating a potential merger between Pfizer Inc. and Pharmacia Corp., the FTC alleged a market including various potential branded drugs for the treatment of erectile dysfunction.[74] Similarly, the FTC alleged a market for the research and development of second-generation oral and intravenous antiviral drugs for the treatment of herpes during the proceedings over the merger of Glaxo Wellcome and SmithKline Beecham.[75] Other alleged markets have related solely to one

69. *See* CONG. BUDGET OFFICE, *supra* note 29, at 23.
70. *Id.* at 23.
71. U.S. DEP'T OF HEALTH & HUMAN SERVS., OUTCOMES AND UTILIZATION FOR HOSPICE AND NON-HOSPICE NURSING FACILITY DECEDENTS, App. A, 4 (2000), *available at* http://aspe.hhs.gov/daltcp/reports/oututil.pdf.
72. Morse, *supra* note 31, at 643-44.
73. *See id.* at 644-52.
74. Complaint ¶¶ 6, 20(c), 24, *In re* Pfizer Inc. & Pharmacia Corp., No. C-4075 (Fed. Trade Comm'n Apr. 11, 2003), *available at* http://www.ftc.gov/os/2003/04/pfizercmp.htm.
75. Complaint ¶ 16(b), *In re* Glaxo Wellcome plc & SmithKline Beecham plc, No. C-3990 (Fed. Trade Comm'n Dec. 15, 2000), *available at* http://www.ftc.gov/os/2000/12/glaxosmithklinecmp.pdf; *see also* COMMENTARY ON THE HORIZONTAL MERGER GUIDELINES, *supra* note 26, at 29-30 (describing this merger among those in which monopolies may encompass one or more markets).

mechanism of action,[76] specific chemical compound,[77] and individual dosage strengths.[78]

What might appear as inconsistent market definition methodologies may instead reflect different competitive realties. As stated earlier,[79] the analysis of market power is context-specific. That competition among branded drugs is based largely on nonprice factors means that the traditional price-based models used by the federal agencies to evaluate mergers may not yield valid results.[80] Market definition may also change over a drug's life cycle. Prior to patent expiry or during a period of regulatory exclusivity, a branded drug manufacturer faces competition from other drugs providing the same or similar therapies.[81] Potential generic competition is only a future concern. If a therapeutic class of drugs or family of drugs with a particular mechanism of action includes no generic substitutes, then the relevant product market for a merger case might include all branded versions in that class or family, or a branded drug product may be sufficiently unique or differentiated to constitute its own market. Finally, toward the end of a drug's life cycle, when generics have supplanted some or all of a branded drug manufacturer's

76. Complaint ¶ 7, *In re* Amgen Inc. & Immunex Corp., No. C-4056 (Fed. Trade Comm'n July 12, 2002), *available at* http://www.ftc.gov/os/2002/07/amgencomplaint.pdf.
77. *See, e.g.*, Complaint ¶¶ 14, 16-20, *In re* Baxter Int'l & Wyeth, No. C-4068 (Fed. Trade Comm'n Dec. 20, 2002), *available at* http://www.ftc.gov/os/22002/12/baxter_wyethcomplaint.pdf. The FTC noted that the companies were "the two leading U.S. suppliers of Pancuronium, a neuromuscular blocking agent," and the proposed merger would create "a duopoly in the market for the manufacture and sale of Pancuronium." *Id.* at ¶ 16.
78. Complaint ¶¶ 6, 11, 16, *In re* Biovail Corp. & Elan Corp., No. C-4057 (Fed. Trade Comm'n Aug. 15, 2002), *available at* http://www.ftc.gov/os/2002/08/biovalcmp.pdf. The market in this case was comprised solely of the generic version of each dosage strength.
79. *See supra* part A.
80. Stephen A. Stack, Jr., *Afterword: Some Further Observations on the Pharmaceutical Wars*, 71 ANTITRUST L. REV. 705, 709-11 (2003).
81. *See, e.g.*, J.B.D.L. Corp. v. Wyeth-Ayerst Labs., No. 01-704, 2005 U.S. Dist. LEXIS 11676, at *23-24 (S.D. Ohio 2005) (relevant market defined to include non-AB-rated oral estrogen replacement therapy products).

sales, the appropriate market may be confined to generics AB rated to each other. Notably, in two recent complaints, the FTC defined the relevant markets to be comprised solely of AB-rated generics of a particular drug molecule.[82]

3. Innovation Markets

While the *Horizontal Merger Guidelines* primarily examine the potential competitive effects of a proposed merger on price, they also note that a firm with market power "may lessen competition on dimensions other than price, such as product quality, service, or innovation."[83] "Innovation markets" delineate competition in the form of research and development for potential goods and services.[84]

82. In *In re* Ivax Corp., 119 F.T.C. 357 (1995), the FTC evaluated the potential merger of two generic manufacturers by examining the impact on the market for the "sale of generic verapamil." In *Biovail/Elan*, the FTC's complaint alleged relevant markets comprised of "30 mg dosages of generic Adalat and . . . 60 mg dosages of generic Adalat." Complaint ¶ 6, Dkt. No. C-4057 (Fed. Trade Comm'n Aug. 15, 2002), *available at* http://www.ftc.gov/os/2002/08/biovalcmp.pdf. In addition, recent cases have recognized that generics of a molecule, excluding the brand, may constitute their own market. *See, e.g.*, Morton Grove Pharms. v. Par Pharm., No. 04-C-7007, 2006 U.S. Dist. LEXIS 13779, at *24 (N.D. Ill. 2006) (sustaining market comprised of "megestrol acetate oral suspension products and/or the generic submarket."); Fed. Trade Comm'n v. Mylan Lab., 62 F. Supp. 2d 25, 54-55 (D.D.C. 1999) (sustaining market of generic lorazepam and clorazepate for monopolization claim, citing massive price increase following a generic drug manufacturer's efforts to keep rival generics off market); *see also, e.g.*, *In re* Lorazepam & Clorazepate Antitrust Litig., 467 F. Supp. 2d 74, 86 (D.D.C. 2006) (same).

83. HORIZONTAL MERGER GUIDELINES, *supra* note 3, § 0.1 n.6.

84. There has been much debate over whether innovation markets are or should be cognizable in the antitrust context. *See, e.g.*, Gilbert & Sunshine, *supra* note 60. Advocates of the cognizability of such markets point to Judge Learned Hand's comment in *Alcoa* that "rivalry is a stimulant, to industrial progress" to show the antitrust laws' concern for innovation. United States v. Aluminum Co. of Am., 148 F.2d 416, 427 (2d Cir. 1945); *see also* Fed. Trade Comm'n v. PPG Indus., 798 F.2d 1500, 1505 (D.C. Cir. 1986) (noting that merging parties competed within prospective markets for future technologies each was researching). Opponents of "innovation markets" deride them as speculative and contend "there is a conceptual, statutory bar against antitrust concern with 'markets' in which no products exist and no one buys or sells property." Ronald W. Davis, *Innovation Markets and Merger Enforcement: Current Practice in Perspective*, 71 ANTITRUST L.J. 677, 678 (2003) (citing Robert J. Hoerner, *Innovation Markets: New Wine in Old Bottles?*, 64 ANTITRUST L.J. 49, 56-57 (1995)).

The 1995 DOJ and FTC's Antitrust Guidelines for the Licensing of Intellectual Property contains a formal definition of innovation markets:

> An innovation market consists of the research and development directed to particular new or improved goods or processes, and the close substitutes for that research and development. The close substitutes are research and development efforts, technologies, and goods that significantly constrain the exercise of market power with respect to the relevant research and development, for example by limiting the ability and incentive of a hypothetical monopolist to retard the pace of research and development. The Agencies will delineate an innovation market only when the capabilities to engage in the relevant research and development can be associated with specialized assets or characteristics of specific firms.[85]

The FTC has challenged several prospective mergers due to concerns that the merged entity would monopolize research and development for the treatment of various diseases.[86]

85. U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, ANTITRUST GUIDELINES FOR THE LICENSING OF INTELLECTUAL PROPERTY ¶ 3.2.3 (1995), *available at* http://www.usdoj.gov/atr/public/guidelines/0558.htm.

86. *See* Complaint ¶ 19, *In re* Pfizer Inc. & Warner-Lambert Co., Dkt. No. C-3957 (Fed. Trade Comm'n June 19, 2000) (relevant market consisting of "the research, development, manufacture and sale of EGFr-tk inhibitors for the treatment of cancer."), *available at* http://www.ftc.gov/os/2000/06/pfizercmp.htm; Complaint ¶ 6, *In re* Baxter Int'l, Dkt. No. C-3726 (Fed. Trade Comm'n Mar. 24, 1997) (research, development, manufacture and sale of fibrin sealant), *available at* http://www.ftc.gov/os/1997/03/c3726cmp.pdf; Complaint ¶¶ 14-19, *In re* Ciba-Geigy Ltd., Dkt. No. C-3725 (Fed. Trade Comm'n Mar. 4, 1997) (innovation in gene therapy

D. Conclusion

Courts and litigants continue to debate whether the traditional market definition method or the use of direct evidence is the most appropriate manner to assess market power. The ultimate goal, however, remains the same: the creation of an analytical framework that best reflects the competitive questions at issue and can assess potential anticompetitive effects.

products), *available at* http://www.ftc.gov/os/1997/04/c3725cmp.pdf; Complaint, *In re* Upjohn Co., 121 F.T.C. 44, 45 (1996) (research, development, manufacture and sale of topoisomerase inhibitors for treatment of colorectal cancer); Complaint, *In re* Glaxo plc, 119 F.T.C. 815, 816 (1995) (research and development of non-injectable $5HT_{1D}$ agonists).

CHAPTER IV

PHARMACEUTICAL MERGERS

A. Merger Review Process

The HSR Act requires parties to a transaction that meet certain size thresholds to file a notification with the FTC and the DOJ and to observe a preclosing waiting period. The HSR Act is a procedural statute designed to give the U.S. antitrust authorities prior notice of economically significant transactions and the opportunity to challenge such transactions prior to their consummation.[1]

The parties to a negotiated transaction are permitted to file their HSR Notification and Report Forms (HSR Forms) after a letter of intent, memorandum of understanding, or definitive agreement is executed, as long as they certify a good faith intention to complete the notified transaction.[2] For a nonnegotiated transaction (e.g., a tender offer or open market purchase),[3] the acquiring person may file its HSR Form after it has provided the requisite notice to the target company, and in the case of a tender offer, has announced publicly its intention to make the offer.[4]

There is no deadline for submitting the HSR Forms, but the parties are prohibited from closing the transaction until the statutory waiting period ends. For negotiated transactions, the waiting period begins to run after each party to the transaction has submitted completed HSR Forms and required documentary attachments. In the case of a nonnegotiated transaction, the waiting period begins after the acquiring party submits its completed HSR filing.[5] The acquiring person must pay a filing fee to the FTC, the amount of which is based upon the value of

1. 15 U.S.C. § 18a. Although both the DOJ and the FTC have jurisdiction to review and investigate proposed mergers under the HSR Act, only one of the agencies will conduct the investigation of a proposed transaction. Pharmaceutical transactions are typically reviewed in the first instance by the staff attorneys of the Mergers I Division at the FTC.
2. 16 C.F.R. § 803.5(b).
3. *Id.* § 801.30(a).
4. *Id.* § 803.5(a).
5. 15 U.S.C. § 18a(b)(1)(A); 16 C.F.R. § 803.10(a).

Administration Amendments Act of 2007 (FDAAA).[217] As a result of the FDAAA, the FDA may not delay the approval of an NDA or ANDA simply because a citizen petition has been filed, unless it determines that a delay is necessary to protect the public health.[218] The FDAAA further provides that if the FDA determines "that a petition . . . was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination."[219] The FDAAA also establishes a 6-month timeframe in which the FDA must respond to petitions that have the potential to affect the approval of any pending application; and, this timeframe is not to be extended for any reason.[220]

E. New Drug Formulations and Product Switching Strategies

Another area that has drawn antitrust attention involves actions taken by the pharmaceutical manufacturer of a branded product to shift the market to a new product in anticipation of the prospective launch of a generic substitute for the existing product. A typical case alleges the following fact pattern: Anticipating generic competition for a brand product, the name brand manufacturer develops a new product—for example, a new formulation or molecular form of the existing active ingredient—to serve the same patient population (i.e., with the same or related indications). The name brand manufacturer then takes steps to shift the market over to the new product.

Unless an NDA is withdrawn for reasons of safety or effectiveness, withdrawal of a drug product from the market does not prevent approval of a generic's ANDA.[221] Withdrawal, however, affects the operation of the generic substitution laws described in Chapter I. Under most state pharmacy laws, a pharmacist may (and sometimes must) fill a prescription for a branded drug with an approved generic substitute,

217. Pub. L. No. 110-85, § 914(a), 121 Stat. 823, 953-57 (2007) (codified at 21 U.S.C. § 355(q)).
218. *See* 21 U.S.C. § 355(q)(1)(A).
219. *Id.* § 355(q)(1)(E).
220. *Id.* § 355(q)(2).
221. *See* 21 C.F.R. § 314.122(c).

unless the prescribing physician expressly directs to the contrary. Generic substitution is allowed only if the generic has been "AB-rated," which means that the generic drug must be both bioequivalent and have the same form, dosage, and strength as the branded drug.[222] These requirements mean that a pharmacist receiving a prescription for the new branded product will not be permitted to substitute the generic form of the old branded product because they are not AB-rated. A few courts have begun to wrestle with the antitrust issues relating to product switching in the pharmaceutical industry, but clear guiding principles have yet to emerge.

1. Legal Standard for Assessing Product Improvements

Uncertainty over the antitrust standard by which new product introductions are to be judged extends well beyond the pharmaceutical industry. One line of authority, springing from the Second Circuit's decision in *Berkey Photo, Inc. v. Eastman Kodak Co.*,[223] argues that determining whether a new product represents an improvement should be left to the marketplace, and any new product introduction should be lawful unless accompanied by coercion (including, potentially, simultaneous withdrawal of a prior product that creates such coercion), predatory pricing, or other antitrust abuse that interferes with consumer choice. As the Second Circuit stated:

> The only question that can be answered is whether there is sufficient demand for a particular product to make its production worthwhile, and the response, so long as the free choice of consumers is preserved, can only be inferred from the reaction of the market. . . . If a monopolist's products gain acceptance in the market, therefore, it is of no importance

222. FOOD & DRUG ADMIN., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, vi (27th ed. 2007) (the "*Orange Book*"); Abbott Labs. v. Teva Pharms., 432 F. Supp. 2d 408, 415 (D. Del. 2006).
223. 603 F.2d 263 (2d Cir. 1979).