DEREGULATING DIRECT-TO-CONSUMER MARKETING OF PRESCRIPTION DRUGS: EFFECTS ON PRESCRIPTION AND OVER-THE-COUNTER PRODUCT SALES*

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Abstract

This paper examines the impact and interrelationships between direct-to-consumer (DTC) and physician-oriented marketing on the sales composition of the prescription (Rx) and over-the-counter (OTC) versions of antiulcer and heartburn medications. To understand better the implications for competition of the 1997 Food and Drug Administration's policies regarding DTC marketing, as well as recent Rx-to-OTC switch approvals, we also examine the relationship between order-of-entry effects and marketing intensities. We find spillover effects of marketing for Rx drugs on same-brand OTC versions of the drugs. We also find that the ratio of cumulative marketing intensity (cumulative marketing efforts divided by cumulative sales) in the OTC segment increases monotonically with order of entry. Our regression results show that various marketing demand elasticities depend on order of entry. Our findings document the importance of nonprice competition in the OTC drug market and suggest that the recent deregulation of Rx DTC marketing enhances rivalry and facilitates competition.

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I. INTRODUCTION

THE effects of marketing efforts on consumer choice and well-being have long been controversial among economists, marketing analysts, and public policy makers. Classic debates include the following: Do marketing efforts generate informational and educational value for consumers, which enables them to make more informed choices? Do marketing efforts exploit informational asymmetry between producers and consumers, increase perceived product differentiation, and induce inefficient rent-seeking behavior by producers? Or do both of these effects hold, varying by product and stage in the product life cycle?[1] These issues are at the heart of current debates concerning the welfare effects of recent regulatory changes at the U.S. Food and Drug Administration (FDA) regarding direct-to-consumer (DTC) marketing for prescription (Rx) drugs.[2]

In 1997, the FDA clarified guidelines on DTC marketing of Rx drugs that allow manufacturers to place both the drug's name and the condition that the drug treats in an advertisement without requiring manufacturers to include all the additional safety and efficacy information that are traditionally found in the product insert.[3] Prior to this change, whenever a drug's brand name appeared in an advertisement, such detailed product insert information was required as well.

Recent years have also seen an acceleration in the number of Rx-only to over-the-counter (OTC) (Rx-to-OTC) switches that have been approved by the FDA.[4] In the 14-year period between 1976 and 1989, the FDA approved 39 Rx-to-OTC switches (about 2.8 per year), but between 1990 and 1996,

[1] See, for example, Federal Trade Commission, Advertising for Over-the-Counter Antacids: Final Staff Report and Recommendations (1983); Mark A. Hurwitz & Richard E. Caves, Persuasion or Information? Promotion and the Shares of Brand Name and Generic Pharmaceuticals, 31 J. Law & Econ. 299 (1988); Keith B. Leffler, Persuasion or Information? The Economics of Prescription Drug Advertising, 24 J. Law & Econ. 45 (1981); Richard L. Schmalensee, The Economics of Advertising (1972); and Richard L. Schmalensee, Product Differentiation Advantages of Pioneering Brands, 72 Am. Econ. Rev. 349 (1982).

[2] See, for example, Ronald S. Bond & David F. Lean, Sales, Promotion, and Product Differentiation in Two Prescription Drug Markets: Staff Report of the Bureau of Economics of the Federal Trade Commission (1977); Marcel P. Gemperli, Rethinking the Role of the Learned Intermediary: The Effect of Direct-to-Consumer Advertising on Litigation, 284 JAMA 2241 (2000); Jane E. Henney, Challenges in Regulating Direct-to-Consumer Advertising, 284 JAMA 2242 (2000); Alison J. Huang, The Rise of Direct-to-Consumer Advertising of Prescription Drugs in the United States, 284 JAMA 2240 (2000); National Survey of Consumer Reactions to Direct-to-Consumer Advertising, Prevention Mag. 8 (1999); Meredith Rosenthal *et al.*, Demand Effects of Recent Changes in Prescription Drug Promotion, in 6 Frontiers in Health Policy Research (Alan M. Garber & David M. Cutler eds. 2003); and Michael S. Wilkes, Robert A. Bell, & Richard L. Kravitz, Direct-to-Consumer Prescription Drug Advertising: Trends, Impact and Implications, 19 Health Aff. 110 (2000).

[3] Manufacturers are required to direct the audience to another source (for example, a toll-free number or a Web site) to obtain additional safety and efficacy information.

[4] For FDA comments on switches, see Tamar Nordenberg, Now Available without a Prescription, FDA Consumer Magazine (1996) (http://www.fda.gov/fdac/features/996_otc.html).

20 switches occurred (about 3.3 per year). Between 1994 and 1996 alone, the FDA approved 10 Rx-to-OTC switches, including Children's Advil, Children's Motrin, Orudis KT, and Actron for pain relief; Femstat 3 for treating vaginal yeast infection; Pepcid AC, Tagamet HB, Zantac 75, and Axid AR for heartburn; and Rogaine for promoting hair growth. Many of today's leading selling OTC products had an Rx heritage. For example, OTC medications such as Advil, Motrin IB, Benadryl, and NyQuil were originally Rx-only drugs that switched to OTC status in the 1980s.[5] The increase in approvals of Rx-to-OTC switches reflects in part the impact of those advocating greater consumer choice, self-medication, and consumer empowerment. It also likely reflects manufacturer incentives as embodied in the Waxman-Hatch Act of 1984, which in some cases permits an additional 3 years of marketing exclusivity for previously Rx-only products whose new approved efficacy indications involve an OTC formulation.

The clarified DTC advertising guidelines provide manufacturers even greater inducements for Rx-to-OTC switches. Specifically, by marketing the Rx version of a drug directly to consumers while it is still under patent protection, a producer may be able to exploit spillovers to its subsequent OTC version, particularly when marketing signals quality and translates into long-lived brand-name equity. Hence, DTC marketing of a branded Rx product may have long-term effects on the subsequent success of Rx-to-OTC switches.

In this paper, we examine recent DTC marketing efforts and Rx-to-OTC switches involving the H_2-antagonist class of drugs, which treats a wide variety of gastrointestinal disorders including duodenal and gastric ulcers, hypersecretory conditions, acid indigestion, and heartburn. These top-selling Rx medications all switched from Rx to OTC in 1995–96—Pepcid to Pepcid AC, Tagamet to Tagamet HB, Zantac to Zantac 75, and Axid to Axid AR. The Rx version of Tagamet lost patent protection in 1994, as did Rx Zantac in 1997, Rx Pepcid in 2001, and Rx Axid in 2002. For some of these drugs, DTC advertising has been used for both the Rx and OTC formulations.

In this paper, we first assess whether order-of-entry effects, documented to be strong in the H_2 Rx market, are also present in the H_2 OTC segment and examine whether there is any carryover of order of entry from the Rx

[5] For further discussion, see Davina C. Ling, Advertising, Competition, and Prescription-to-Nonprescription Drug Switches in the US Antacid Market (unpublished Ph.D. dissertation, Massachusetts Inst. Tech., June 1999); Barbara Hesselgrave, Will Managed Care Embrace Rx-to-OTC Switches? Drug Topics, June 2, 1997, at 13; Robert McCarthy, OTCs: The Wild Card in Cost-Effectiveness, 17 Bus. Health 33 (1999); Mickey C. Smith, Rx-to-OTC Switches: Reflections and Projections, Drug Topics, July 20, 1998, at 70; Bruce Stuart & James Grana, Are Prescribed and Over-the-Counter Medicines Economic Substitutes? A Study of the Effects of Health Insurance and Medicine Choices by the Elderly, 33 Med. Care 487 (1995); and Elyse Tanou & Thomas M. Burton, More Firms "Switch" Prescription Drugs to Give Them Over-the-Counter Status, Wall St. J., July 29, 1993, at B1.

to the OTC markets.[6] Next we consider the role of DTC marketing, as well as traditional physician-oriented "detailing" marketing, on the sales composition of the OTC H_2s and of the Rx H_2s. Finally, we assess whether there are any significant interactions between the Rx and OTC DTC marketing efforts for a brand.

As best we can determine, the research we report here is the first systematic empirical examination of the impact and interrelationships between DTC marketing on Rx and OTC versions of "sunset" branded pharmaceuticals facing Rx patent expiration.[7] Our research integrates data from various sources, such as Rx drug sales and marketing data from IMS Health, scanner OTC data from Information Resources, Incorporated (IRI), as well as DTC marketing data from Leading National Advertisers. We begin with a historical overview of regulatory and other factors affecting the Rx and OTC H_2-antagonist products.

II. Background

As early as the 1800s, patent medicine advertisers were the largest patrons of newspaper advertising.[8] The modern distinction between Rx and OTC drugs began with the 1938 Federal Food, Drug, and Cosmetic Act, which defined different labeling guidelines for Rx and OTC drugs. Under the 1938 act, even though the authority over the labeling of both Rx and OTC drugs was given to the FDA, control over drug marketing remained with the Federal Trade Commission. The 1962 Kefauver-Harris amendments to the Federal Food, Drug, and Cosmetic Act gave the FDA its current responsibility for monitoring Rx drug promotional materials. The 1962 amendments outlined basic requirements for Rx marketing: Rx promotional materials cannot be false or misleading; they must provide a "fair-balance" coverage of risks and benefits of using the drug; they must provide a summary of contraindications, side effects, and effectiveness; and they must also meet specific guidelines for readability and size of print.

[6] See Ernst Berndt *et al.,* Information, Marketing and Pricing in the U.S. Anti-ulcer Drug Market, 85 Am. Econ. Rev. 100 (1995); Ernst Berndt *et al.,* The Roles of Marketing, Product Quality and Price Competition in the Growth and Composition of the U.S. Anti-ulcer Drug Industry, in The Economics of New Goods 277 (Timothy F. Bresnahan & Robert J. Gordon eds. 1997).

[7] For related empirical research on Rx-to-OTC switches, see Peter Temin, Costs and Benefits in Switching Drugs from Rx to OTC, 2 J. Health Econ. 187 (1983); Peter Temin, Realized Benefits in Switching Drugs, 35 J. Law & Econ. 351 (1992); and Ernst R. Berndt, Margaret K. Kyle, & Davina Ling, The Long Shadow of Patent Expiration: Generic Entry and Rx-to-OTC Switches, in Scanner Data and Price Indexes 229 (Robert C. Feenstra & Matthew D. Shapiro eds. 2002). Additional research on order-of-entry effects in Rx pharmaceutical markets is Ernst Berndt *et al.,* An Analysis of the Diffusion of New Antidepressants: Variety, Quality and Marketing Efforts, 5 J. Mental Health & Pol. Econ. 3 (2002).

[8] James Harvey Young, The Medical Messiahs: A Social History of Health Quackery in Twentieth Century America (1967), as cited in Wilkes, Bell, & Kravitz, *supra* note 2.

Since then, Rx drugs have been marketed not only to physicians, but also more directly to consumers. As noted by Ernst Berndt and coauthors,[9] for example, in March 1988 Tagamet Rx launched "Tommy Tummy" and "stomach TLC" DTC marketing campaigns, and soon after Glaxo initiated an extensive television and print DTC effort for Zantac. Under the interpretation of FDA regulations regarding DTC marketing at that time, the marketing was quite restrictive in that if a brand name was mentioned in the advertisement, extensive product-labeling information was required to accompany the advertisement.

These restrictions on DTC marketing were relaxed and clarified in 1997 when the FDA issued new draft guidelines. A manufacturer is now permitted to advertise an Rx drug's name and the condition for which it is indicated without needing to issue as fully detailed a summary regarding the product's side effects and other risks. The FDA requirements for risk disclosure in advertisements may be met if the advertisements contain information on the product's main risks and refer to other sources from which consumers may obtain additional product information and full product labeling. For instance, a prominently positioned toll-free phone number (or Web address) must now be found on the advertisement, which the consumer can use to obtain further information. Usually, there is explicit encouragement for readers and viewers of DTC advertisements to discuss the product with their physicians.

While relatively little is known to date regarding the ultimate impacts of DTC marketing of Rx products on consumer utilization and health status,[10] there is little doubt that relaxation of the DTC restrictions by the FDA has been associated with a very substantial increase in DTC marketing of Rx products. In particular, according to IMS Health, DTC marketing expenditures for Rx medications increased from $1.1 to $2.5 billion between 1997 and 2000.[11]

Both the shift in regulatory regime for DTC advertising and the more favorable regulatory environment for Rx-to-OTC switches are important in explaining recent developments in the H_2-antagonist market. The first H_2-antagonist, Tagamet (chemical name, cimetidine), was introduced in 1977. It revolutionized the treatment of ulcers by allowing pharmacological treatment on an outpatient basis, rather than with expensive inpatient care such as hospital stays and surgeries. Three other H_2-antagonists were launched between 1983 and 1988: Zantac (ranitidine), Pepcid (famotidine), and Axid (nizatidine). The benefits of patent protection, together with successful marketing and the resulting widespread utilization, led to spectacular revenue

[9] Berndt *et al.*, The Roles of Marketing, *supra* note 6.

[10] For an initial and preliminary analysis, see Prevention Mag., *supra* note 2. Also see Wilkes, Bell, & Kravitz, *supra* note 2; and Meredith Rosenthal *et al.*, Promotion of Prescription Drugs to Consumers, 346 New Eng. J. Med. 498 (2002).

[11] IMS Health data can be obtained at http://www.imshealth.com. Also see Rosenthal *et al.*, *supra* note 2.

sales growth for the Rx-only H_2s. In the early to mid-1990s, Zantac was the most widely prescribed and the highest-sales-volume Rx drug in the United States, and Tagamet was among the top 10 best-selling Rx medications.

Although the introductions of the Rx H_2s marked the beginning of new medical treatments for gastrointestinal disorders, the H_2s were not spared from the forces of creative destruction. In 1989, new and more potent drugs for the treatment of ulcers and gastroesophageal reflux disease (GERD), namely, the proton pump inhibitors (PPIs), were introduced. This latest generation of drugs has a convenient once-a-day dosing regimen and very few side effects. Even at the time of its initial approval in May 1995, the manufacturer of one of the PPIs (Prevacid) was able to claim superiority in its labeling and promotion over ranitidine (then the best-selling and most prescribed H_2) for the treatment of heartburn. By 1997, the PPIs had overtaken the H_2s as the largest-revenue-generating Rx drugs in the United States (and the world).

Besides confronting intense competition from the PPIs in the 1990s, the H_2s also faced the threat of Rx patent expiration and imminent generic entry. Tagamet's patent expired on May 17, 1994, followed by the loss of Zantac's market exclusivity in late July 1997.[12] Drug manufacturers may benefit from Rx-to-OTC switches because in certain cases they can gain the limited additional market exclusivity granted by the Waxman-Hatch Act of 1984. This provision allows pioneer manufacturers an extra 3 years of market exclusivity provided that the manufacturer obtains FDA approval for a new presentation and indication for a chemical entity.[13] Expecting loss of patent protection in the mid-1990s, for example, beginning as early as 1985, SmithKline discussed with the FDA the possibility of seeking and gaining approval for an OTC version of Tagamet to treat heartburn.[14]

With this as background, we proceed with the remainder of this paper as follows. In Section III, we provide a brief literature review and examine important concepts for the Rx and OTC markets. In Section IV, we discuss data sources and the construction and interpretation of various price, quantity, and marketing measures, first for Rx drugs and then for OTCs. In Section

[12] See Berndt, Kyle, & Ling, *supra* note 7; Berndt *et al.*, Information, Marketing and Pricing, *supra* note 6; and Berndt *et al.*, Roles of Marketing, *supra* note 6, for a more detailed discussion of the historical development in the H_2-antagonist market.

[13] Empirical analyses of the effect of the Waxman-Hatch Act include those by Henry G. Grabowski & John M. Vernon, Brand Loyalty, Entry, and Price Competition in Pharmaceuticals after the 1984 Drug Act, 35 J. Law & Econ. 331 (1992); Richard E. Caves, Michael D. Whinston, & Mark A. Hurwitz, Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry, Brookings Papers on Economic Activity: Microeconomics 1 (1991); and Richard G. Frank & David S. Salkever, Generic Entry and the Pricing of Pharmaceuticals, 6 J. Econ. Mgmt. 75 (1997). For a historical overview of FDA regulation of the drug industry prior to 1980, see Peter Temin, Taking Your Medicine: Drug Regulation in the United States (1980).

[14] For a Harvard Business School case study discussion of the race to develop and launch the first OTC H_2-antagonist in the United States, see Charles King III *et al.*, Pepcid AC(A): Racing to the OTC Market (2000).

V, we present evidence on the importance of order-of-entry effects in the OTC market for H_2-antagonists and assess the extent of order-of-entry spillovers from the Rx heritage to the OTC market. In Section VI, we formulate, and then provide empirical evidence for, a relatively simple set of econometric models quantifying the effects of DTC and traditional detailing on shares among the Rx and OTC H_2-antagonists. Finally, in Section VII we summarize and conclude.

III. Literature Review and Conceptual Considerations

The market for Rx drugs involves complex interactions among pharmaceutical companies and regulators as well as among patients, physicians, pharmacists, third-party payers, and policy makers. Physicians act as agents for their patients and in that capacity prescribe drugs for them. Since physicians choose among competing drugs, and because of historical restrictions on advertising to patients, until recently most marketing efforts for Rx drugs have been directed at physicians, both in the form of visits by sales representatives to physicians (detailing) and by print advertising in medical journals. Previous studies, such as those by Berndt and coauthors,[15] have shown that along with other factors, such physician-directed marketing efforts in the Rx market have had a substantial sales impact and are long-lived.

Moral hazard likely affects sales in the Rx market, for patients with Rx drug coverage typically make copayments that are considerably less than the total payment for the Rx, with the third-party insurers responsible for most of the cost. Other things equal, this insurance-induced wedge between patient copayments and total payments for a Rx undoubtedly increases demand for Rx drugs.[16]

The roles of principal-agent issues and moral hazard are likely to be much smaller in the OTC than in the Rx market. Over-the-counter drugs are typically inexpensive relative to brand-name Rx drugs, although consumers usually bear the total costs out-of-pocket because third-party insurance rarely reimburses for OTC drugs. Since many OTC (and, for that matter, Rx) products are primarily "experience" rather than "search" goods, brand loyalty is strong, which perhaps reflects consumers' idiosyncratic responses to medications, risk aversion, and/or imperfect information. Thus, even for OTC products, perceived switching costs may be high despite their relatively low cost.[17] Once consumers experience benefits from use of a particular OTC

[15] Berndt *et al.,* Information, Marketing and Pricing, *supra* note 6; and Berndt *et al.,* Roles of Marketing, Product Quality and Price Competition, *supra* note 6.

[16] For more discussion of this point, see Ernst R. Berndt, The U.S. Pharmaceutical Industry: Why Major Growth in Times of Cost Containment? 20 Health Aff. 100 (2001).

[17] For a classic discussion of search and experience goods and the importance of their distinction in understanding marketing efforts, see Philip K. Nelson, Advertising as Information, 82 J Pol. Econ. 729 (1974). Additional discussion of decision making in the OTC market is found in Ling, *supra* note 5.

medication, they may be reluctant to experiment with alternative OTC products. Consumers may be less informed than medical professionals regarding the efficacy and appropriate uses of various OTC medications. In such ways, risk aversion and imperfect information may raise switching costs and confer important roles on brand names, which signal quality. As noted by Richard Schmalensee[18] and others, high switching costs and imperfect information can lead to first-mover, or at least order-of-entry, advantages to incumbents.

Ronald Bond and David Lean,[19] Berndt and coauthors,[20] and Charles King and coauthors[21] have documented strong order-of-entry effects in the branded Rx H_2-antagonist market. Within OTC and other nonmedication consumer markets, there is a large literature documenting the importance of order of entry for pioneering brands; surveys are given by Glen Urban and coauthors[22] and William Robinson and coauthors.[23]

To date, there is no empirical evidence on the spillover of order of entry in Rx markets onto the OTC market. In the current context, it is worth emphasizing that Zantac was able to overcome Tagamet's first-mover advantage in the Rx market in part by employing aggressive marketing efforts that conveyed information on Zantac's claimed advantages—more convenient daily dosing, fewer side effects, and fewer adverse interactions with other drugs than Tagamet. Although their product profiles were more like Zantac than Tagamet, third Rx entrant Pepcid and fourth Rx entrant Axid were not able to overcome their late-entrant disadvantages. As we discuss in more detail in Section V, order of entry in the OTC market differed from that in the Rx segment; in the OTC segment, Pepcid AC was first entrant, then Tagamet HB, Zantac 75, and finally Axid AR. While the time gap between first and second entrants was only about 2 months in the OTC market, in the Rx market it was 6 years.

Davina Ling[24] notes that unlike in the Rx market, most private labels, minor brands, and other drugs in the OTC market do not need to seek specific approvals from the FDA before marketing, so long as they meet good manufacturing practice and other drug regulatory standards. For off-patent products having approved active ingredients, OTC drugs encounter relatively minor barriers to entry. In spite of this, OTC markets for, say, gastrointestinal (GI) and pain remedies are relatively concentrated, with old brand names

[18] Schmalensee, Product Differentiation Advantages, *supra* note 1.

[19] Bond & Lean, *supra* note 2.

[20] Berndt *et al.*, Information, Marketing and Pricing, *supra* note 6; and Berndt *et al.*, Roles of Marketing, *supra* note 6.

[21] King *et al.*, *supra* note 14.

[22] Glen Urban *et al.*, Market Share Rewards to Pioneering Brands: An Empirical Analysis and Strategic Implications, 32 Mgmt. Sci. 645 (1986).

[23] William T. Robinson, Gurumurthy Kalyanaram, & Glen L. Urban, First-Mover Advantages from Pioneering New Markets: A Survey of Empirical Evidence, 9 Rev. Indus. Org. 1(1994).

[24] Ling, *supra* note 5.

still dominating sales. For example, as early as the 1970s, the OTC GI remedies market was already dominated by eight major brands, which accounted for approximately 80 percent of the market revenue share. Similarly in 1995, OTC drugs such as Tylenol and Advil, more than 20 years old, still achieved combined sales of more than $1.2 billion.

Consistent with the endogenous sunk-cost theory proposed by Sutton,[25] the OTC drug market has traditionally been dominated by a few major brands that invested heavily in marketing and a small competitive fringe with numerous firms and low marketing investments. In particular, in 1977, the average advertising/retail sales ratio for the eight major brands in the OTC GI remedies market was approximately 21 percent.[26] Direct-to-consumer marketing has continued to play an important role in the more recent OTC GI remedies market. For the seven largest-selling antacid OTC products, between 1990 and 1996 the median advertising/retail sales ratio was approximately 34 percent.[27]

While first-mover advantages are considerable, they may not be insurmountable. Entrants who invest heavily in marketing and who can differentiate their products from the pioneer may overcome the incumbent's edge. In such cases, the information content of marketing efforts reduces switching costs by informing consumers of other, possibly more effective, alternative medications. In this context, deregulation of DTC marketing of Rx products can play an important role in reducing order-of-entry advantages to pioneers, thereby increasing nonprice competition among early and later entrants. How such deregulation of DTC marketing of Rx products spills over into same-brand advantages in the subsequent OTC market is not clear, however. Our modest goal in this paper is to identify and quantify such impacts, if they exist.

In evaluating the impacts of DTC marketing on Rx and OTC versions of H_2-antagonists, we expect the marginal product of marketing to vary over the product life cycle. For example, for new products, marketing may convey important incremental information, attracting new users and raising consumer awareness of the product and its uses (particularly when the medical condition is underdiagnosed and undertreated), thereby increasing the size of the market being served. However, for mature products for which consumers have already developed strong preferences and high levels of brand loyalty, and particularly when the market has been saturated, the social marginal product of additional marketing may be much smaller, even though the private mar-

[25] John Sutton, Sunk Costs and Market Structure (1991).

[26] Federal Trade Commission, *supra* note 1.

[27] Ling, *supra* note 5. The seven brands are Tums, Mylanta, Gaviscon, Maalox, Alka Seltzer, Rolaids, and Pepto Bismol.

ginal product for each participant may be positive. This is consistent with the market expansion and "market-stealing" effects of marketing.[28]

IV. Data Sources, Descriptions, and Interpretations

Empirical research on interactions among Rx drug and OTC markets at the time of patent expiration requires integrating data from a number of diverse sources. We now briefly summarize our data sources. We begin with Rx drugs and then move on to the OTCs.

A. Prescription Drug Markets

Price, quantity, revenue, and marketing data for antiulcer and heartburn Rx drugs are taken from IMS Health, monthly from January 1988 through June 1999. IMS's Retail Perspective tracks monthly shipments from manufacturers and wholesalers to retail warehouses and outlets. The revenue data are those to manufacturers and wholesalers, and not to the retail outlets (who add retail margins). Although revenues are net of charge backs (discounts given to purchasers and channeled through wholesalers), rebates (payments made to providers who often do not take title to the pharmaceuticals, for example, managed care organizations) are not included in the IMS revenue data, and neither are prompt payment discounts. The exclusion of rebates from the revenue data implies an overstatement of Rx revenues and prices, but the extent of this overstatement is unknown, for data on rebates tend to be highly proprietary. In spite of this drawback in the IMS data, however, many branded and generic pharmaceutical companies purchase and utilize the IMS data for their internal research.

The level of aggregation of the IMS retail purchase data is at the presentational form, for instance, bottles of 30 tablets each having a 150-mg strength. We convert these various presentational sales measures into quantity or unit data by using the recommended daily dosage for active duodenal ulcer treatment as the transformation factor. The resulting quantity data can then be interpreted as the hypothetical patient-days of therapy per month if all patients were taking the recommended active duodenal ulcer daily dosage.[29] Data on recommended daily dosages are taken from the *Physicians' Desk Reference*.[30] Price per day of therapy is then computed as revenues divided by the quantity of therapy days in that month. Further details on

[28] Also see Berndt *et al.,* Information, Marketing and Pricing, *supra* note 6; and Berndt *et al.,* Roles of Marketing, *supra* note 6, for an analysis of market expansion versus competitive effects of marketing in the Rx H_2 market.

[29] The transformation factors are Tagamet (cimetidine), 800 mg/day; Zantac (ranitidine), 300 mg/day; Pepcid, 40 mg/day; and Axid, 300 mg/day.

[30] Physicians' Desk Reference (2000).

price, quantity, and revenue measurement are found in the data appendix of Berndt and coauthors.[31]

The price, quantity, and revenue data we employ cover only sales into drugstores. While drugstore sales constitute on average about 70–80 percent of sales in all outlets, the data exclude sales to hospitals, long-term care facilities, and mail order distributors.[32] Since hospital usage and marketing differs considerably from the outpatient environment, we confine our attention here to the traditional retail sector.

To measure marketing efforts involving pharmaceutical sales representatives' (detailers') physician office visits, we employ IMS Health data from their Office Contact Report. On the basis of a panel of about 3,800 physicians who report the number of visits and minutes spent with detailers discussing particular products, IMS extrapolates monthly detailing efforts by drug to the national level. Using an estimated cost per detailing visit, IMS also estimates total detailing expenditures.

Medical journal advertising pages and expenditures are estimated by IMS in their National Journal Audit. The universe measured by this audit includes journal pharmaceutical advertising directed to those in all types of medical practice, including pharmacists, nurses, podiatrists, and dentists as well as medical and osteopathic practitioners. On the basis of circulation, the number of square inches and pages of advertisements, and the copy characteristics such as premium positioning and the number of colors in each advertisement, IMS uses standard rate sheets from over 300 major medical journals to estimate total dollars of journal advertising by drug on a monthly basis. Further details on these marketing measures can be found in the data appendix of Berndt and coauthors[33] and in IMS Health's *Information Services Manual*.[34]

Data on DTC marketing of Rx brands from Leading National Advertisers (LNA)/Media Watch Multi-Media Service is published on a quarterly basis by Competitive Media Reporting.[35] This service reports Rx brand advertising expenditure estimates in 10 major media: consumer magazines, Sunday magazines, newspapers, outdoor, network television, spot television, syndicated television, cable television, network radio, and national spot radio. The LNA/Media Watch Multi-Media Service includes only brands of companies spending a total of $25,000 or more year-to-date in the 10 media measured. The data we employ report advertising expenditures by company and then list brands for each company. Currently, our DTC data are available through the second quarter of 2000. We gathered quarterly Rx brand advertising data for the companies selling the branded H_2s. To transform the quarterly data into

[31] Berndt *et al.*, The Roles of Marketing, *supra* note 6.

[32] IMS Health, Information Services Manual (1998).

[33] Berndt *et al.*, The Roles of Marketing, *supra* note 6.

[34] IMS Health, *supra* note 32.

[35] Now called TNS Media Intelligence/CMR. See http://www.tnsmi-cmr.com.

monthly periodicity, we employed the STATA command ipolate.[36] The monthly expenditure data were then deflated by the Bureau of Labor Statistics (BLS) Advertising Agency Producer Price Index to convert them into constant-dollar figures.[37]

B. Over-the-Counter Drug Markets

The quantity, price, and revenue data used to analyze the OTC H_2 market are taken from InfoScan and are based on store-level optical scanner data that are purchased and collected from multiple retail outlets by IRI.[38] These scanner data are collected weekly from more than 29,000 chain drugstores, mass merchandisers, food stores, and chain convenience stores located in major metropolitan areas and rural areas. They are then projected to national levels for these chains. The IRI data provide detailed information on sales, pricing, and promotion on a stock-keeping unit basis. The volume of sales is recorded for each package size of each brand on an average weekly basis. The weekly data are aggregated to the monthly level.

Since our research goal is to examine interactions between the Rx and OTC markets, we need to establish comparable units of consumption. For each OTC brand, we aggregate the data across presentations and regional outlets so that the quantity measure reflects the total milligrams sold each month nationally. For instance, if 5,000 packages of Tagamet HB each having 25 tablets of 200 mg cimetidine are sold, we compute the total number of milligrams of Tagamet HB sold that month as $5{,}000 \times 25 \times 200 \text{ mg} = 25 \times 10^6$ mg. The IRI data record sales from drugstores, mass merchandisers, and food stores to consumers and therefore include both wholesale and retail margins, unlike the IMS Health data for Rx sales. Another important distinction between these data sources is that the IMS data reflect inventory-stocking behavior by, for example, chain drugstore warehouses, while the IRI data include only actual sales to final consumers.

To make the quantity units of the various OTC H_2 brands comparable to each other and comparable to the Rx H_2 brands, we normalize the total number of milligrams per brand sold each month by the Rx daily dosage recom-

[36] See STATA Reference Manual, STATA Reference Manual Release 6 (1999).

[37] For July 1995 onward (when the deflators first became available), we constructed this deflator as the arithmetic average of the Bureau of Labor Statistics, Producer Price Index for "Advertising agencies, ad creation, billed separately," and "Advertising agencies, media placement, including ad creation not billed" (http://www.bls.gov). For months prior to July 1995, we employed the Producer Price Index for "All finished goods."

[38] See Information Resources, Inc., Store Data Measures (1997); Peter M. Guadagni & John D. C. Little, A Logit Model of Brand Choice Calibrated on Scanner Data, 2 Marketing Sci. 203 (1983); and Randolph E. Bucklin & Sunil Gupta, Commercial Use of UPC Scanner Data: Industry and Academic Perspectives, 18 Marketing Sci. 247 (1999). The IRI Web address is http://www.infores.com.

mended to treat active duodenal ulcers.[39] Although we describe our quantity measure as patient-days of therapy, in fact this is not literally true.[40] Rather, the quantity measures should be interpreted as the number of patient-days of therapy that would be consumed hypothetically if all the OTC H_2s were used for the treatment of active duodenal ulcers at recommended Rx dosages. It is worth emphasizing here that this is a theoretical construct, and we do not wish to imply or suggest that any or all patients actually (mis)use the OTC H_2s to treat active duodenal ulcers.[41] We make this transformation solely for the purpose of standardizing units of active ingredient.

Once quantity units are calculated, we divide total revenues by quantity, thereby obtaining a price per patient-day of therapy. It is useful to note that both the revenue and price OTC data reflect the impacts of periodic "sales" and discounts, as well as the effects of coupons redeemed by consumers at the time of the retail transaction.

To obtain measures of monthly advertising of OTC H_2s, we again employ data from LNA/Media Watch Multi-Media Service. LNA distinguishes consumer-oriented OTC brand advertising from that for Rx brands. Quarterly data on media advertising over the 10 media mentioned earlier for the H_2 OTC brands are taken from Class D213, Over-the-Counter Digestive Aids and Antacids. The ipolate command in STATA is again employed to convert expenditure data from quarterly to monthly. Monthly advertising expenditures in current dollars are then deflated by the BLS's Producer Price Index for Advertising Agencies, as discussed above.

V. Order of Entry, Marketing Efforts, and Market Shares in the Over-the-Counter H_2 Market

The four branded H_2s all entered the OTC market within 13 months of one another—first Pepcid AC in June 1995, followed by Tagamet HB in August 1995, Zantac in April 1996, and, finally, Axid AR in July 1996. Would Pepcid AC be able to fully exploit the potential first-mover advantages it had achieved? How would subsequent entrants fare? What would be the impact of Rx order of entry on the OTC market? Here we report results of an initial analysis of order-of-entry effects. We first analyze the relationship between the advertising/sales ratio and order-of-entry effects. We then describe sales developments for the OTC H_2s by examining factors affecting the monthly revenue sales and revenue shares among the four OTC H_2s.

[39] This follows procedures utilized by Ling, *supra* note 5.

[40] Recommended dosages vary by indication. For example, while the recommended dosage of Zantac for treating active duodenal ulcers, active gastric ulcers, and gastroesophageal reflux disease is 300 mg per day (either 300 mg once daily or 150 mg twice daily), the recommended dosage for duodenal ulcer maintenance therapy is only 150 mg per day.

[41] For each of the four OTC H_2s, the transformation of OTC to Rx involves using twice the maximum daily recommended OTC dosages.

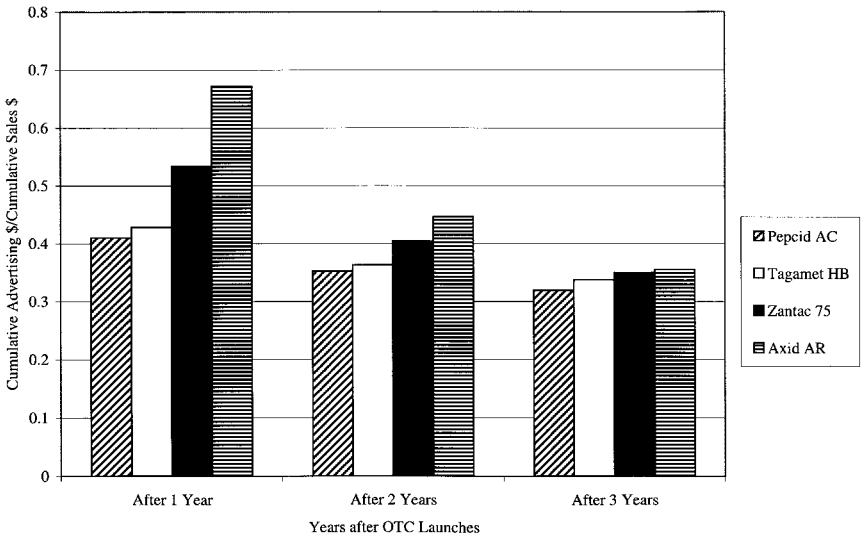

FIGURE 1.—Cumulative detailing/sales ratios by over-the-counter (OTC) drug

Order-of-entry effects can manifest themselves in a number of ways, one of which involves advertising intensity. In the Rx H_2 market, for example, 1, 2, and 3 years after initial launch, marketing/sales ratios (cumulative detailing minutes divided by cumulative units sold) were smallest for the pioneer and were successively higher for each subsequent Rx H_2 entrant.[42] This finding is consistent with the theory of first-mover advantage and consumer switching costs in the Rx market.

To construct a comparable marketing/sales ratio for the OTC H_2 market, we compute cumulative advertising dollar expenditures (summed over the 10 advertising media) for each OTC H_2 and divide this by cumulative OTC H_2 revenues for each of the 3 years following launch.[43] Figure 1 presents the rather striking results for the OTC market. Later entrants have successively higher advertising/sales ratios. The ratio for Pepcid AC, the pioneer, is .41 in the year of launch. For Tagamet HB, the second entrant, it is .43; Zantac 75 and Axid AR have ratios of .53 and .67, respectively. Since advertising efforts are particularly intense immediately following product launch, it is not surprising that all four advertising/sales ratios decline over time. The

[42] See figure 7.7, p. 293, in Berndt *et al.*, Roles of Marketing, *supra* note 6.

[43] We present advertising/sales ratio as opposed to the level of advertising because of Dorfman and Steiner's insight that the profit-maximizing combination of price and advertising level for firms with market power is one whereby the advertising/sales ratio is equal to the ratio of the advertising elasticity of demand to the price elasticity of demand; see Robert A. Dorfman & Peter O. Steiner, Optimal Advertising and Optimal Quality, 44 Am. Econ. Rev. 826 (1954).

relationship between order of entry and the advertising/sales ratio persists 2 years after launch: first-mover Pepcid AC has the lowest value (.35), while the followers have higher ratios (.36 for Tagamet HB, .40 for Zantac 75, and .45 for Axid AR). Although the order-of-entry ranking persists 3 years after launch, the differences in the advertising/sales ratio among the four entrants diminish considerably over time: .32 for pioneer Pepcid AC, .34 for second entrant Tagamet HB, .35 for third entrant Zantac 75, and .36 for last entrant Axid AR. This reduction in differences over time is not surprising, since relative time on the market converges for the four OTCs with the passage of time.

This monotonic relationship between the advertising/sales ratio and order of entry supports the notion that consumers incur a switching cost for OTC medications, which is consistent with a first-mover advantage. This may also help explain the need for later entrants to invest more heavily in marketing to overcome incumbents' advantages. We examine the rationale behind the relationship between order of entry and marketing intensity further in Section VI.

An important aspect of rivalry in the Rx H_2 market involved the indications for which the FDA granted approval. Zantac Rx, for example, was the first H_2 to obtain approval for GERD (a severe form of heartburn), and having this approval allowed Zantac Rx detailers to expand their marketing efforts significantly by visiting offices of general practitioners and internists, not just the smaller number of gastroenterologists who treated ulcers. In the OTC H_2 market, a different but related rivalry developed that also involved FDA indication approvals. In April 1995, pioneer Pepcid AC received FDA approval not only for the treatment of episodic heartburn, but also for its prevention. Thus Pepcid AC could be marketed as a preemptive treatment that was used prior to eating spicy foods, for example. By contrast, when Tagamet HB received its initial FDA approval in June 1995, it was for the relief of symptoms of occasional heartburn, acid indigestion, and sour stomach, but not for their prevention. This placed Tagamet HB at a competitive disadvantage in its ability to market. The demand for preventative medication was likely to be very large, but Tagamet HB was preempted from marketing itself for prevention until it received a similar FDA approval for prevention on November 15, 1995.

In addition to its indication disadvantage, for Tagamet HB the initial dose was two 100-mg tablets, whereas the Pepcid AC dose was only one 10-mg tablet; in November 1996, Tagamet HB was able to change this to one 200-mg tablet per dose. Zantac 75 received FDA approval for only the relief of heartburn on December 19, 1995, while Axid AR received approval on May 9, 1996, for only the prevention of meal-induced heartburn, acid indigestion, and sour stomach.[44] Pepcid AC thus enjoyed two first-mover advantages in

[44] See the U.S. Food and Drug Administration, Approved Drug Products with Therapeutic

the OTC market: it was the first H_2 to obtain OTC approval from the FDA and the first to obtain approval for the prevention of heartburn, not just symptomatic relief. Although this dual first-mover advantage might have provided considerable benefits to Pepcid AC, the time differences in launch dates among the four OTCs were relatively small, and thus Pepcid AC may not have been able to exploit them as well as it would have if launch dates had been spread out over greater time intervals.

To describe sales developments for the OTC H_2s since their launch in 1995–96, we plot monthly days of therapy for each of the OTC H_2s in Figure 2, along with corresponding revenue shares in Figure 3. In interpreting these figures, recall first that the OTC prices are actual average consumer prices paid at mass merchandisers, food stores, and drugstores that use scanner checkout equipment and sell their chain store data to IRI. Thus, sales from convenience and other stores that do not employ scanner data are not included in the IRI data; also excluded are sales from stores that have scanning equipment but that are not part of chains selling their data to IRI. This implies that the OTC quantity and revenue data understate total U.S. sales. Second, in August 1996, at $1.60 and $1.53, Zantac 75 and Axid AR average daily prices were considerably higher than those for Pepcid AC ($1.31) and Tagamet HB ($1.26). As the average number of tablets per package increased over time, average daily prices fell for all four OTCs. By July 1999, there was little price dispersion: the average price for Axid AR was $1.09; for Zantac 75, $1.12; for Tagamet HB, $1.14; and for Pepcid AC, $1.16.

With this in mind, we now examine monthly sales units and revenue shares. As is seen in Figure 2, order-of-entry effects were apparently important in the OTC market, but they were not entirely invincible. First entrant Pepcid AC had been the market leader ever since its launch in June 1995, and last entrant Axid had sustained apparently permanent last-mover disadvantages. However, Zantac 75 was able to overtake Tagamet HB, the second mover in the OTC market, within 2 months of Zantac's launch. Zantac was unable to translate its Rx success into surmounting Pepcid AC's 10-month first-mover and indication approval advantages. In short, we observe some positive spillover effects from the Rx-to-OTC markets, but these appear to be limited.

A second result depicted in Figure 2 is that the OTC market for H_2s has become a large one. At the end of our sample in mid-1999, the four OTC products accounted for about 38 million patient-days of therapy per month (a figure biased downward for reasons discussed above), compared with about 70 million patient-days of Rx H_2 therapy sold to drugstores. Over-the-counter sales of the branded H_2s have therefore become a quite substantial component of brand equity, but the importance of OTC sales differs by brand. Over-the-counter patient-days of Pepcid AC therapy were about half those of

Equivalence Evaluations, in Electronic Orange Book (June 2000) (http://www.fda.gov/cder/ob/default.htm), for FDA approval dates of Rx and OTC versions of the drugs.

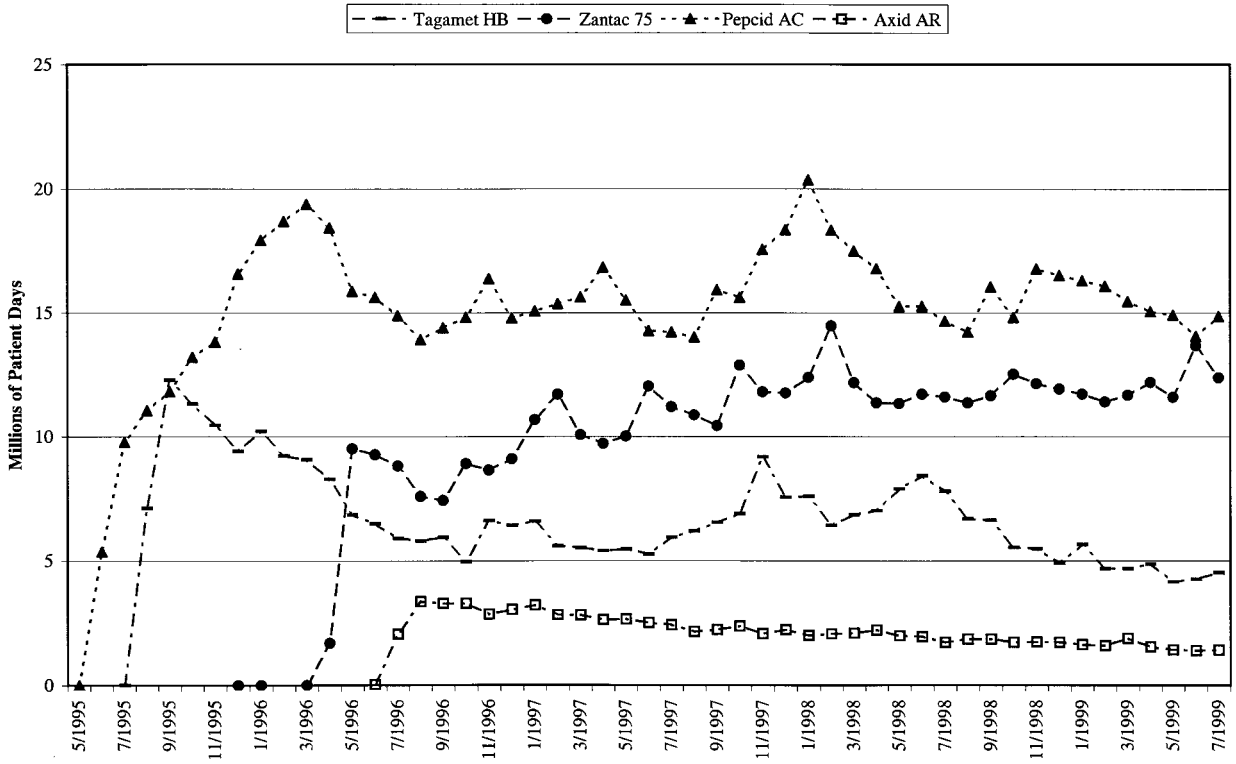

FIGURE 2.—Units of over-the-counter H_2 antagonists, monthly

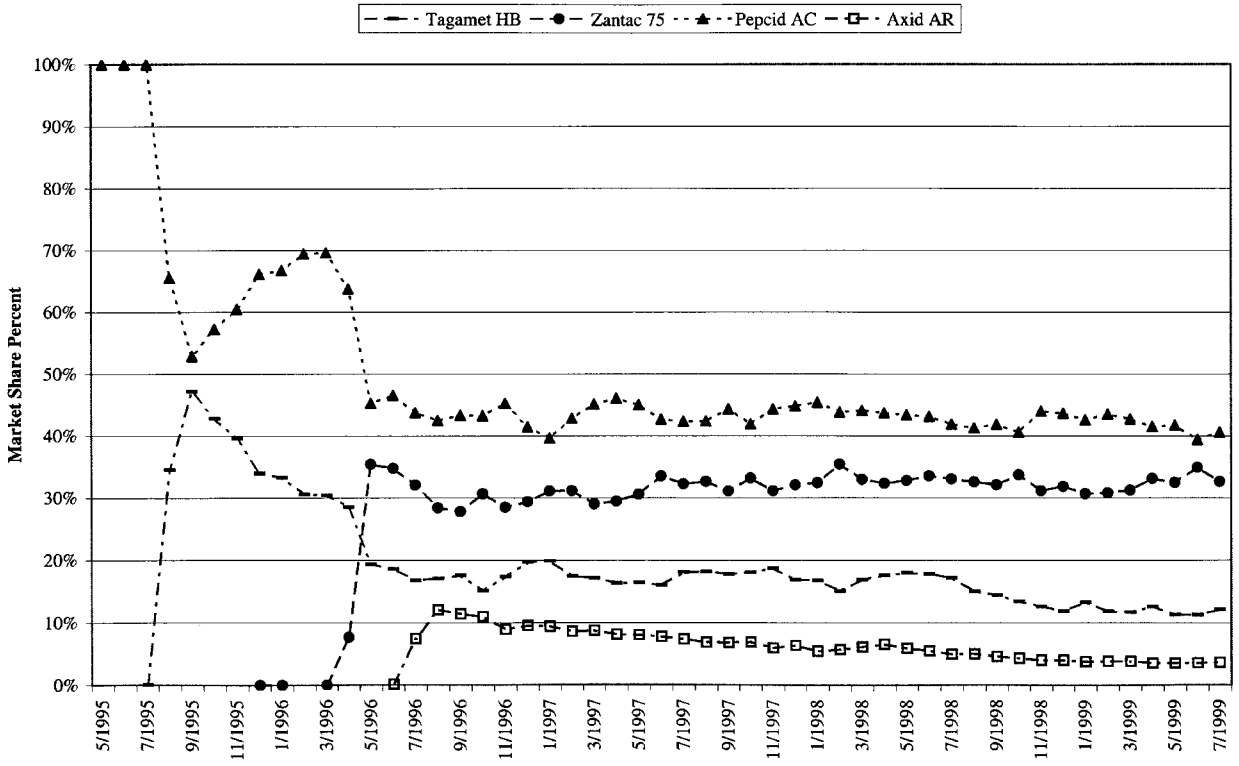

FIGURE 3.—Revenue shares of over-the-counter H_2 antagonists

Pepcid Rx. However, total days of therapy for Zantac 75, Tagamet HB, and Axid AR were only about 25–40 percent of those of their Rx (branded plus generic) sales. For Zantac and Tagamet, this implies brand equity that can persist even after the Rx product loses patent protection.

In Figure 3, we plot revenue shares for the four branded OTC H_2s. Given the information conveyed in Figure 2, it is not surprising that the revenue share of Pepcid AC was largest, hovering around 45 percent ever since mid-1996. The revenue share for Zantac 75 ranged from 28 percent to slightly under 35 percent and generally increased slowly but unsteadily over time. The launches of Zantac 75 and Axid AR appear to have hurt Tagamet HB. At the end of the sample time period in mid-1999, the Tagamet HB revenue share was about 12 percent, while that for Axid AR was 3–4 percent.[45]

We find, therefore, that order-of-entry and positive spillover effects between Rx and OTC brands contributed to success in the OTC market. Later entrants appeared to employ marketing instruments to mitigate earlier-entrant advantages. We assess this order-of-entry effect further in the regression analyses reported below. Consumer switching costs, imperfect information, and risk aversion may explain the high level of brand loyalty in the OTC drug market. Indeed, if asymmetric information and risk aversion are important in explaining high consumer switching costs, then Rx-to-OTC switches may be a good way to overcome the incumbent informational advantage in the OTC market. Specifically, by marketing the Rx version of a drug directly to consumers, producers may be able to exploit spillovers to its OTC version if the effects of advertising and brand-name capital are long-lived or signal quality. However, since we do not have data that would permit us to examine the informational content of marketing, detailed discussions of the informational value of marketing are outside the scope of this paper.

VI. Econometric Models of Impacts of Direct-to-Consumer Drugs and Traditional Marketing in the Prescription and Over-the-Counter H_2 Markets

With this descriptive analysis of order-of-entry effects, marketing efforts, and realized market shares of the OTC products as background, we now formulate testable hypotheses regarding the relationship between order of entry and marketing efforts. According to the Dorfman-Steiner[46] theorem, when profit-maximizing firms face downward-sloping demand curves, the optimal price and marketing efforts occur where the ratio of dollar marketing to sales equals the ratio of the marketing elasticity of demand to the (absolute value of the) price elasticity of demand. In the previous section, we reported that the cumulative advertising/sales ratios increased monotonically with or-

[45] The remaining market is composed of private-label OTC cimetidine.

[46] Dorfman & Steiner, *supra* note 43.

der of entry. If the price elasticities of demand were similar for all four products (or perhaps even greater for later entrants), then it follows that the marketing elasticity of demand must also increase with order of entry.

The above hypothesis may appear counterintuitive at first glance, but the intuition underlying the larger OTC DTC marketing elasticities for later entrants, ceteris paribus, is relatively simple. Let f_1' and f_2' be the marginal products of marketing for the first and second entrants, respectively. By definition, the marketing elasticity of demand can be written as $\alpha_i^M = f_i'(A_i/q_i)$, where A_i represents the level of marketing efforts and q_i represents the units sold for entrant i. If we evaluate entrants 1 and 2 at a common level of marketing efforts, then $\alpha_2^M > \alpha_1^M$ if and only if $f_2'/f_1' > q_2/q_1$. We would indeed expect $q_2 < q_1$ from first-mover advantages. If later entrants face smaller "penalties" in relative marginal product of marketing than in relative units sold, then $f_2'/f_1' > q_2/q_1$, and in that case later entrants will have larger marketing elasticities of demand (holding marketing efforts constant). Combined with the Dorfman-Steiner theorem and holding other things equal, we would then expect the marginal product from marketing efforts to become smaller for later entrants, as well as the marketing elasticity of demand to increase with order of entry. We examine the above hypothesis by adding interaction terms between marketing stocks and the order-of-entry variable to the traditional econometric demand model specification (see equations (2) and (3) below).

The underlying conceptual framework for our econometric analysis is very simple, and it is implicit rather than explicit. We build from the traditional economic theory of demand, mindful that in the Rx market, principal-agent issues involving physicians and patients and moral hazard resulting from the presence of insurance coverage complicate matters considerably.

In each of our regressions, we specify quantity demanded as a function of price, marketing efforts, and other factors. It is reasonable to expect that marketing efforts are long-lived, having sales impacts far beyond the month in which they are incurred. In previous research, it has been common to assume that the rate of depreciation of the impact of marketing efforts on sales is constant over time. We follow that tradition here, although research that generalizes the depreciation rate to allow it to increase as patent expiration approaches deserves high priority. We specify the marketing stock Z_t as a weighted sum of previous monthly marketing expenditure flows. According to the perpetual inventory method,

$$Z_t = (1 - \delta)Z_{t-1} + M_t, \tag{1}$$

where δ is the monthly depreciation rate and M_t is the new marketing expenditure incurred during month t. Thus, the marketing stock at the end of month t is the depreciation-adjusted amount from the previous period plus this month's new (inflation-adjusted) marketing efforts. If $\delta = 0$, then Z_t is simply the cumulative sum of all previous real marketing efforts, and if

$\delta = 1$, then the effects of this period's marketing efforts completely disappear at the end of the month and $Z_t = M_t$. In the econometric implementation, we estimate δ, rather than assume an a priori value. Further, we allow for different depreciation rates for DTC and physician-oriented marketing. Finally, we estimate demand models allowing price, quantity, and marketing all to be jointly determined, using instrumental variable methods.

A. Shares within Over-the-Counter Drugs

As a first step, we begin with factors affecting choice among the OTCs. The panel of OTC brands is an unbalanced one because of the different dates of product launch; for each OTC brand, the data end in May 1999. Although theoretical developments in the economic theory of demand now permit empirical specifications in which the number of alternative goods in the choice set changes over time, empirical implementations (based on multinomial logit or generalized extreme-value distributions) are few because of their computational complexity.[47] We follow the marketing and order-of-entry literature in which it has been traditional to specify the dependent and explanatory variables all relative to the pioneer in an unbalanced panel framework.[48]

Let QDAYOTC_{jt} be the number of days of therapy for OTC brand j in month t; PDAYOTC_{jt}, the corresponding price; ZOTCDTC_{jt}, the marketing stock of OTC marketing of brand j via DTC media; ZRXDTC_{jt}, the marketing stock of the Rx version of OTC drug j marketing on the basis of DTC media; and ZRXMD_{jt}, the marketing stock of the Rx version of OTC drug j marketing on the basis of physician-directed media. We define OTCORDER_j as the order of entry of OTC drug j in the OTC H_2 market, $\text{OTCORDER}_j \times \log(\text{ZRXMD}_j)$ as the interaction term between OTC order of entry and the log of relative physician-directed advertising stock of Rx drug j, $\text{OTCORDER}_j \times \log(\text{ZRXDTC}_j)$ as the interaction term between order-of-entry and the log of relative DTC advertising stock of Rx drug j, and $\text{OTCORDER}_j \times \log(\text{ZOTCDTC}_j)$ as the interaction term between order of entry and the log of relative advertising stock of OTC drug j to that of Pepcid AC. Given that the model framework involves variables measured relative to the first entrant, Pepcid AC, OTCORDER_j takes on values 2, 3, and 4.

[47] See, for example, Steven Berry, James Levinsohn, & Ariel Pakes, Automobile Prices in Market Equilibrium, 63 Econometrica 841 (1995); and Timothy F. Bresnahan, Scott Stern, & Manuel Trajtenberg, Market Segmentation and the Sources of Rents from Innovation: Personal Computers in the Late 1980s, 28 Rand J. Econ. S17 (1997).

[48] See Berndt *et al.*, Information, Marketing and Pricing, *supra* note 6; and Berndt *et al.*, Roles of Marketing, *supra* note 6.

We specify a regression equation having the form[49]

$$\begin{aligned}\ln\left(\frac{\text{QOTCDAY}_{jt}}{\text{QOTCDAY}_{\text{PAC},t}}\right) = {} & a_0 + a_1 \times \ln\left(\frac{\text{POTCDAY}_{jt}}{\text{POTCDAY}_{\text{PAC},t}}\right) \\ & + a_2 \times \ln\left(\frac{\text{ZOTCDTC}_{jt}}{\text{ZOTCDTC}_{\text{PAC},t}}\right) \\ & + a_3 \times \ln\left(\frac{\text{ZRXDTC}_{jt}}{\text{ZRXDTC}_{\text{PAC},t}}\right) \\ & + a_4 \times \ln\left(\frac{\text{ZRXMD}_{jt}}{\text{ZRXMD}_{\text{PAC},t}}\right) \\ & + a_5 \times \text{OTCORDER}_j \\ & + a_6 \times \text{OTCORDER}_j \times \ln\left(\frac{\text{ZOTCDTC}_{jt}}{\text{ZOTCDTC}_{\text{PAC},t}}\right) \\ & + a_7 \times \text{OTCORDER}_j \times \ln\left(\frac{\text{ZRXDTC}_{jt}}{\text{ZRXDTC}_{\text{PAC},t}}\right) \\ & + a_8 \times \text{OTCORDER}_j \times \ln\left(\frac{\text{ZRXMD}_{jt}}{\text{ZRXMD}_{\text{PAC},t}}\right) + \varepsilon_{jt},\end{aligned} \tag{2}$$

where PAC is the OTC pioneer Pepcid AC; j = Tagamet HB, Zantac 75, or Axid AR; and ε_{jt} is a random error term. Notice that the proportional effect of, say, a relative change in DTC marketing for an OTC product on its log market share in this interaction specification is equal to $a_2 + a_6 \times \text{OTCORDER}_j$, and thus the effect of relative DTC marketing of an OTC product depends on that product's order of entry in the OTC market. Consistent with our hypotheses, we expect a_6 to be positive such that later entrants would face higher relative OTC DTC marketing demand elasticities. While we expect the marginal effect of order of entry on OTC demand to be negative (namely, later entrants have lower market shares than earlier entrants), we do not have any a priori assumptions regarding the signs of a_7 and a_8 (that is, the signs of the marginal effect of OTC order of entry on the cross-marketing elasticity of Rx drugs).

We "stack" the Tagamet HB, Zantac 75, and Axid AR observations, estimate the unbalanced panel by nonlinear least squares (NLS), and employ procedures to adjust for heteroskedasticity in standard errors.[50] Since by

[49] Results from initial regressions yielded unsatisfactory estimated coefficients on various variables capturing new FDA indication and dosing approvals for the OTC drugs. Since the differences in FDA indication approvals may already be captured by variations in advertising and pricing, and since the time differences between product launches were relatively minor, we excluded these FDA-related variables from further consideration.

[50] The sample size is 175 for NLS.

equation (1) the marketing stock variables depend on an unknown monthly deterioration rate δ, we perform a two-dimensional grid search over δ from 0 percent to 30 percent separately for physician-oriented and DTC marketing stocks, in steps of .5 percent, and then choose as our preferred model that combination of the δs and the remaining parameters that minimizes the mean square error.[51]

The within-OTC share model employs IRI scanner data for the OTC H_2s, IMS Health data on Rx physician-oriented marketing, and LNA data on DTC marketing of OTC and Rx products.

Column (1) of Table 1 shows the NLS regression results. The price elasticity is estimated to be -1.622 and is negative and significant ($p < .001$). The estimated monthly depreciation rates (on the basis of the grid search procedure) for physician-directed media and consumer-directed media are 10 percent and 13 percent, respectively. Relative OTC quantities demanded are positively related to physician-directed marketing stocks of their Rx brands with an elasticity that varies significantly with the order of entry.

Although the estimate of a_2 is insignificant, $a_2 + a_6 \times \text{OTCORDER}_j$ (that is, the effect of DTC marketing of the OTC drug on its demand) is positive and significant at all relevant values of OTCORDER_j. The relative OTC DTC marketing elasticities for OTC Tagamet, Zantac, and Axid are .176 ($p < .02$), .318 ($p < .001$), and .460 ($p < .001$), respectively. The estimated relative elasticities of physician-directed marketing stocks are .163 (for Tagamet; $p < .001$), $-.328$ (for Zantac; $p < .001$), and $-.819$ (for Axid; $p < .001$). While there are positive spillovers from Rx physician-oriented marketing to an Rx-to-OTC switch for Tagamet, the spillover effects are negative for Zantac and Axid, which suggests OTC-Rx substitutability and cannibalization of Zantac and Axid OTC sales. In terms of spillovers from DTC marketing of the Rx version of the drug, we find small but still positive and significant spillovers for Zantac and Axid, but negative and insignificant spillovers for Tagamet. The relative elasticities for Zantac and Axid are .068 ($p < .001$) and .144 ($p < .001$), while for Tagamet the relative elasticity of DTC marketing of the Rx drug on OTC drug demand is $-.008$. By itself, the order-of-entry parameter estimate is also strong and significant. A joint *F*-test of the coefficients from the order-of-entry and interaction variables shows that these variables are significant ($p < .001$). Our findings therefore display multifaceted spillovers between marketing for the Rx drug and demand for the same-brand OTC drug. Marketing and order of entry play important roles in this market.

The NLS results are based on the assumption that regressors such as relative

[51] This yields numerically equivalent parameter estimates to an NLS estimator that repeatedly substitutes in for lagged values of $Z_{t-\tau}$ and thereby makes Z_t a weighted power series over all previous marketing flow expenditures. However, the standard errors from this grid search method are likely slightly underestimated.

TABLE 1

PARAMETER ESTIMATES FROM MARKET-SHARE MODELS FOR THE PRESCRIPTION (RX) AND OVER-THE-COUNTER (OTC) MARKETS

	EQUATION (2), OTC MARKET		EQUATION (3), RX MARKET	
	NLS (1)	2SLS (2)	NLS (3)	2SLS (4)
log(relative price)	−1.622** (.283)	−1.947** (.556)	.014 (.036)	−.441** (.061)
log(relative Rx physician-oriented marketing stock)	1.145** (.071)	.663** (.098)	1.467** (.091)	1.677** (.303)
log(relative Rx DTC marketing stock)	−.160** (.024)	−.169** (.023)	−.073** (.016)	−.082 (.067)
log(relative OTC DTC marketing stock)	−.108 (.093)	−.218 (.273)	−.004 (.008)	.012 (.013)
OTCORDER	−1.846** (.178)	−2.179** (.695)		
OTCORDER × log (relative Rx MD-oriented marketing stock)	−.491** (.039)	−.273** (.041)		
OTCORDER × log (relative Rx DTC marketing stock)	.076** (.010)	.072** (.010)		
OTCORDER × log (relative OTC DTC marketing stock)	.142** (.017)	.181** (.069)		
RXORDER			−.385** (.017)	−.330** (.019)
RXOFFPAT			−.002* (.001)	−.001 (.001)
Constant	1.508 (.968)	2.557 (2.786)	.556** (.050)	.409** (.092)
Depreciation rate for physician-oriented marketing (%)	10.0	25.0	.0	1.0
Depreciation rate for DTC marketing (%)	13.0	13.0	32.0	29.0
R^2	.961	.958	.774	.867
N	175	171	552	389

NOTE.—Estimated heteroskedasticity-robust asymptotic standard errors are in parentheses. NLS = nonlinear least squares; 2SLS = two-stage least squares; DTC = direct to consumer; MD = physician.

* Significant at the .05 level.

** Significant at the .01 level.

price and marketing investments are exogenous. But given the monopolistically competitive market structure for these OTC products, both pricing and marketing efforts are unlikely to be exogenously determined variables. Hence, we also estimate parameters in equation (2) using instrumental variables (two-stage least squares (2SLS)) and test for endogeneity using a Hausman specification test.

We employ two sets of exogenous variables as instruments. One group is common to all firms: log of average hourly earnings of production workers in pharmaceutical and advertising industries; log of producer price index of pharmaceuticals, cable television, network television, and outdoor advertising; a time counter; and quarterly indicators. The other group of instruments is firm specific: the number of months the Rx molecule has been off patent relative to the number of months Tagamet has been off patent, order of entry in the Rx market, log of the firm's DTC advertising stock for other non-H_2-antagonist stomach remedies relative to J&J Merck's DTC advertising stock for other non-H_2-antagonist stomach remedies, and log of the firm's DTC advertising stock for non-H_2-antagonist Rx products relative to Merck's DTC advertising stock for non-H_2-antagonist Rx products. We construct these stocks by assuming the monthly advertising depreciation rate to be 5 percent. We find systematic differences in the NLS and 2SLS estimates and reject the hypothesis that NLS is a consistent estimator of parameters in equation (2) ($\chi^2 = 30.91$, $p < .0001$).

Column (2) of Table 1 shows the 2SLS results.[52] The 2SLS and NLS results are generally qualitatively similar although quantitatively different. The price elasticity is estimated to be -1.947 and is negative and significant ($p < .002$). The estimated monthly depreciation rates (on the basis of the grid search procedure) for physician-directed media and consumer-directed media are 25 percent and 13 percent, respectively. The relative OTC quantities that are demanded are positively related to relative DTC marketing stocks for Zantac and Axid, but not for Tagamet. The estimated elasticity is .144 (for Tagamet), .324 (for Zantac, $p < .001$), and .505 (for Axid, $p < .001$). Consistent with Dorfman-Steiner's framework, we find that increasing advertising/sales ratios for later entrants correspond with their facing increasing OTC DTC marketing elasticities. Relative OTC quantities are also positively related to DTC marketing stocks of their Rx brands for Zantac (.047, $p < .001$) and Axid (.119, $p < .001$) but are negative for Tagamet ($-.025$, $p < .01$). On the other hand, relative quantities are negatively related to physician-directed marketing stocks of their Rx brands for Zantac ($-.157$, $p < .001$) and Axid ($-.430$, $p < .001$) but positively and significantly related to physician-directed marketing stocks of Rx Tagamet (.116, $p < .001$). Again, we find strong and significant order-of-entry effects.

[52] The sample size is 171 for 2SLS because data on advertising by the same firm for other products were not always available.

In summary, the various marketing elasticities depend systematically on order of entry. Prescription to over-the-counter spillovers involving both physician-directed and DTC marketing differ in sign depending on order of entry.[53] These multivariate results are consistent with the bivariate descriptive results reported earlier concerning the effects of order of entry on advertising intensity. Specifically, later entrants have higher relative OTC DTC marketing elasticities, and consistent with the Dorfman-Steiner theorem, they also have higher advertising/sales ratios. This is also consistent with the notion that later entrants face lower marginal returns on marketing and hence need to invest more in marketing relative to incumbents in order to reduce order-of-entry disadvantages.

B. Shares within the Prescription H_2 Markets

For the Rx market, we employ a similar approach to that used for the OTCs. Here, Tagamet is the pioneer, and variables for Rx drug *j* are measured relative to Tagamet (cimetidine). Let QRXDAY_{jt} and PRXDAY_{jt} be the quantity and price of a day of Rx therapy for drug *j*, and let RXOFFPAT_{jt} be the number of months the Rx drug has been off patent and faced generic competition; ZRXMD_{jt}, ZRXDTC_{jt}, and ZOTCDTC_{jt} are as defined earlier. We define RXORDER_j as the order of entry of Rx drug *j* in the Rx H_2 market and note that this variable takes on values of 2, 3, or 4.

With these variables defined, we specify the within-Rx H_2 regression as having the form

$$\begin{aligned}\ln\left(\frac{\text{QRXDAY}_{jt}}{\text{QRXDAY}_{\text{CIM},t}}\right) = {} & b_0 + b_1 \times \ln\left(\frac{\text{PRXDAY}_{jt}}{\text{PRXDAY}_{\text{CIM},t}}\right) \\ & + b_2 \times \ln\left(\frac{\text{ZOTCDTC}_{jt}}{\text{ZOTCDTC}_{\text{CIM},t}}\right) \\ & + b_3 \times \ln\left(\frac{\text{ZRXMD}_{jt}}{\text{ZRXMD}_{\text{CIM},t}}\right) \\ & + b_4 \times \ln\left(\frac{\text{ZRXDTC}_{jt}}{\text{ZRXDTC}_{\text{CIM},t}}\right) \\ & + b_5 \times \text{RXORDER}_j \\ & + b_6 \times (\text{RXOFFPAT}_{jt} - \text{RXOFFPAT}_{\text{CIM},t}) + u_{jt},\end{aligned} \tag{3}$$

[53] This hypothesis regarding spillovers involving physician-directed marketing and Rx-to-OTC switches could be explored further using another data set, namely, the National Ambulatory Medical Care Survey, to examine whether physician-directed marketing leads physicians to advise their patients to purchase OTC versions of the drug when it becomes available in non-Rx strength or whether instead physician-directed marketing induces physicians to prescribe Rx versions of the drug even when the non-Rx strength is available. Although the

where u_{jt} is a random error term.[54] We expect b_1 to be negative; namely, we expect relative units sold to vary negatively with relative prices, other things equal, although the presence of Rx drug insurance could dilute the expected negative relationship. We expect b_3 and b_4 to be positive, reflecting positive effects of relative physician-oriented and DTC marketing on relative Rx units sold. We do not have any a priori assumptions about the sign and magnitude of b_2 given the ambiguous spillover effects of DTC marketing of OTC brand on demand for the same-brand Rx drug. Although we expect b_5 to be negative, the expected sign of b_6 is ambiguous because of the combination of order-of-entry effects and generic entry (namely, early entrants generally faced earlier patent expiration).

Again we employ data from IRI, IMS Health, and LNA. Note that the Rx quantity and unit data for the two off-patent H_2s (Zantac and Tagamet) include generic sales. On the basis of a balanced monthly panel from January 1989 through June 2000, we estimate parameters in equation (3) by NLS and 2SLS (using the same instruments as described in the previous section).[55] Columns (3) and (4) of Table 1 report the corresponding results. A Hausman specification test again shows systematic differences in the coefficients from the NLS and 2SLS estimations ($\chi^2 = 162.45$, $p < .001$).

On the basis of the 2SLS specification, the estimated values of the monthly depreciation rate δ for physician-directed and consumer-directed marketing, using the grid search procedure, are 1 percent and 29 percent, respectively. Similar very low depreciation rates for physician-directed Rx marketing have been reported by Berndt and coauthors.[56] On the other hand, DTC marketing efforts depreciate much more rapidly in the Rx H_2 market than in the OTC H_2 segment. The price elasticity estimate of $-.441$ is small in absolute value, which reflects perhaps measurement error in the IMS Health Rx price measures (which exclude rebates) and the fact that prices paid by consumers can vary in ways that differ from price variation at the drugstore level.

These results imply that there appear to be fewer OTC-Rx marketing spillovers in the Rx market than in the OTC segment. Specifically, the relative quantities demanded of Rx H_2s are not significantly related to relative DTC marketing stocks of the same-brand OTC H_2 products nor to relative same-

advantage of this data set is its microeconomic observations (households and individuals), the sample sizes for these specific drugs are likely to be somewhat small, and coding errors between OTC and Rx versions of the same brand could create econometric difficulties. We therefore leave such research for another time.

[54] We did not include interaction terms between order-of-entry variables and marketing stocks because of the difficulty in interpreting those variables given a generic entry for Tagamet and Zantac and because of the greatly reduced role of marketing both preceding and following generic entry. On this, see Berndt, Kyle, & Ling, *supra* note 7.

[55] The sample size is 552 for NLS and 389 for 2SLS because of the lack of data for some of the instruments in the later time periods.

[56] Berndt *et al.*, Information, Marketing and Pricing, *supra* note 6; and Berndt *et al.*, Roles of Marketing, *supra* note 6

Rx-brand DTC marketing, but relative Rx quantities are strongly and positively related to the relative physician-oriented Rx marketing stocks (1.677, $p < .001$). As in Berndt and coauthors,[57] order-of-entry effects are negative and very strong ($-.330$, $p < .001$). Differences in months after loss of Rx patent expiration insignificantly affect the relative quantities demanded.

VII. Summary and Conclusions

The 1997 relaxation of restrictions on DTC marketing of Rx-only drugs in the United States has been accompanied by a substantial increase in DTC marketing efforts. In the mid-1990s there was also a marked increase in the number of previously Rx-only drugs approved by the FDA to be marketed under OTC status. In this paper, we have examined the impacts of DTC marketing, traditional physician-oriented detailing marketing, and other factors in affecting choice among the H_2-antagonist heartburn and antiulcer medications in the Rx-only and OTC markets. We have also examined spillovers between the Rx and OTC segments, as well as the relationship between order-of-entry effects and firms' marketing intensities.

We find that price and nonprice instruments (specifically marketing) play an important role in competitive rivalry among brands in the OTC market. Regarding marketing efforts, we find that DTC marketing of OTC brands has a substantial positive impact on own share in the OTC market segment and that for later entrants such as Zantac and Axid there is a significant and positive impact of DTC marketing of Rx brands on the share of same-brand OTC products. Therefore, deregulation of the DTC marketing of Rx products has spillover effects in the OTC market. Furthermore, for later OTC entrants Zantac and Axid, physician-oriented marketing of Rx brands has a negative and significant but relatively short-lived impact on the share of same-brand OTC products. Thus, for later entrants, physician-oriented Rx marketing cannibalizes their OTC sales. In summary, the sign and magnitude of marketing spillover effects depend on the marketing medium, the target audience, and the order of entry.

In contrast, DTC marketing of the same-brand OTC H_2 products appears to have no significant impact on the market shares for the same-brand Rx products, other things equal. Instead, only the relative physician-oriented marketing efforts of the H_2-antagonist brands have substantial and long-lived impacts on their own Rx shares. Marketing spillovers flow from Rx to OTC, but not from OTC to Rx.

One of the most interesting sets of findings in this study is the similarity of the relationships between order-of-entry effects and marketing intensities in the Rx and OTC market segments. Previous research in the Rx segment has shown that the ratio of cumulative marketing intensity (cumulative mar-

[57] Berndt *et al.*, Information, Marketing and Pricing, *supra* note 6.

keting efforts divided by cumulative sales) in the Rx segment increases monotonically with order of entry—the first entrant having the lowest intensity and successive entrants having higher marketing intensities. We observe the same general relationship in the OTC market. In addition, in the OTC market the magnitude of various marketing demand elasticities depends on their order of entry. An implication of this finding is that nonprice competition is very important in both the Rx and OTC segments. Specifically, while marketing is costly and may be less productive on the margin in increasing sales for later entrants, it is nonetheless an important tool in reducing earlier-entrant advantages. In this way, the deregulation of Rx DTC marketing enhances rivalry and facilitates competition.

Finally, while order-of-entry effects may be significant, they are not insurmountable, and there is some evidence of spillovers between the Rx and OTC markets. In particular, while the second Rx entrant, Zantac, was able to overcome the first-mover advantages of Rx Tagamet in the Rx market, neither of these brands was able to carry over its early-Rx-entrant advantages into a lead for its brand in the OTC market. Instead, first-OTC-entrant Pepcid AC was able to retain its first OTC entrant advantages till the end of our sample period in mid-1999. But over the same time period, the third OTC entrant, Zantac 75, was able to surpass second OTC entrant Tagamet HB and capture the second largest market share.

In future research, it will be useful to assess whether consumption spillovers (involving information obtained by others' consumption of a drug), which are observed in the Rx H_2 market, carry over to the OTC segment.[58] Future research might also usefully focus on modeling the depreciation of marketing efforts, particularly as a function of the age of the product and as patent expiration approaches.[59] Moreover, it would be useful to utilize more fully and explicitly recent developments in the economic theory of consumer demand that allow for consumer preference estimation even when the number of available products changes over time.[60] However, the existence of principal-agent and moral hazard issues, particularly strong in the Rx market, makes such research very difficult.

Finally, a very important set of issues, likely involving even more challenging modeling and measurement problems, involves examining the effects of DTC marketing not only on consumption patterns, but also on the health status of individuals. To the extent DTC marketing provides information of value to individuals concerning the prevalence of ailments and the availability

[58] Consumption externality effects at the individual brand and aggregate H_2 level are analyzed by Ernst R. Berndt, Robert S. Pindyck, & Pierre Azoulay, Consumption Externalities and Diffusion in Pharmaceutical Markets: Antiulcer Drugs, J. Indus. Econ. (forthcoming, 2003).

[59] See Ling, *supra* note 5.

[60] See, for example, Berry, Levinsohn, & Pakes, *supra* note 47; and Bresnahan, Stern, & Trajtenberg, *supra* note 47.

of medications to treat these ailments effectively, the benefits to consumers from deregulation of DTC marketing could be very substantial.

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