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BRAND LOYALTY, GENERIC ENTRY AND PRICE COMPETITION IN PHARMACEUTICALS IN THE QUARTER CENTURY AFTER THE 1984 WAXMAN-HATCH LEGISLATION

Ernst R. Berndt
Murray L. Aitken

Working Paper 16431
http://www.nber.org/papers/w16431

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
October 2010

Paper presented at the Pharmaceutical Economics Conference honoring Professor Henry Grabowski, Durham, North Carolina, Sept. 17, 2010. Research support from the Pharmaceutical Research and Manufacturers of America is gratefully acknowledged, as is the considerable data and technical support from Michael S. Kleinrock and Kevin J. Weiss at IMS Health. The statements, findings, conclusions and opinions contained and expressed herein are based in part on data obtained under license from the following IMS Health Inc. information services: PlanTrak (2006-2009); IMS Health National Prescription Audit; IMS Health NPA Plus 7, Method of Payment; and IMS National Sales Perspectives. Any statements, findings and conclusions are those of the authors, and are not necessarily those of the institutions with whom the authors are affiliated, the research sponsor, or the National Bureau of Economic Research.

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NBER Working Paper No. 16431
October 2010
JEL No. D4,I11,I18,L11,L65

ABSTRACT

The landmark Waxman-Hatch Act of 1984 represented a "grand compromise" legislation that sought to balance incentives for innovation by establishing finite periods of market exclusivity yet simultaneously providing access to lower cost generics expeditiously following patent expiration. Here we examine trends in the first quarter century since passage of the legislation, building on earlier work by Grabowski and Vernon [1992,1996] and Cook [1998]. The generic share of retail prescriptions in the U.S. has grown from 18.6% in 1984 to 74.5% in 2009, with a notable acceleration in recent years. This increase reflects increases in both the share of the total market potentially accessible by generics, and the generic efficiency rate – the latter frequently approaching 100%. Whereas in 1994, the generic price index fell from 100 to 80 in the 12 months following initial generic entry and by 24 months to 65, in 2009 the comparable generic price indexes are 68 and 27, respectively. Recent studies sponsored by the American Association of Retired Persons focus only on brand prices and ignore substitution to lower priced options following loss of patent protection. For the prescription drugs most commonly used by beneficiaries in Medicare Part D, the average price per prescription declined by 21.3% from 2006 to 2009, rather than increasing by 25-28% as reported by the AARP. Finally, we quantify changes over time in the average daily cost of pharmaceutical treatment in nine major therapy areas, encompassing the entire set of molecules within each therapy class, not simply the molecule whose patent has expired. Across all nine therapeutic areas, at 24 months post-generic entry, the weighted mean reduction in pharmaceutical treatment cost per patient is 35.1%.

Ernst R. Berndt
MIT Sloan School of Management
100 Main Street, E62-518
Cambridge, MA 02142
and NBER
eberndt@mit.edu

Murray L. Aitken
Senior Vice President
Healthcare Insight
IMS Health
901 Main Avenue, Suite 612
Norwalk, CT 06851
maitken@imshealth.com

I. INTRODUCTION

Over the four-plus decades since receiving his Ph.D. in economics from Princeton University in 1967, Henry Grabowski, along with numerous distinguished collaborators, has made wide-ranging contributions in industrial organization, the economics of R&D and innovation, and regulatory economics, each having significant influence within the academy, among public policy makers, and on decision making within industry. Although he is best known for his research on the pharmaceutical, biotechnology and vaccine industries, Henry Grabowski has also published in various other areas, such as cost-effectiveness analyses, automobile insurance and safety regulation, the economics of education, and on price and non-price competition in the cigarette industry. It is an honor and a privilege for us to offer this paper on the occasion of Henry's 70th birthday, and at this conference commemorating his numerous achievements.

The wide range of Henry Grabowski's research contributions over the years allows authors such as us the luxury of choosing a focus for our paper, and for that we are grateful. But how is one to choose? One way of classifying Henry's wide range of research contributions and achievements is to break them down into pre- and post-launch, the former including the economics of R&D and innovation (e.g., costs of bringing new products to market, incentives to do R&D), and the latter economic issues during the product life cycle of biopharmaceuticals after launch (e.g., effective patent lives, revenues and costs over the product life cycle, skewed revenues and returns, the effects of the 1984 Drug Price Competition and Patent Term Restoration Act --hereafter, the Waxman-Hatch Act -- on the extent and speed of generic entry, and its impacts on price competition among and between brands and generics). In this paper we will focus on post-launch economics, and in particular on the impacts of the Waxman-Hatch Act, taking advantage of the quarter century of data that has accumulated since 1984 passage of that landmark legislation. Notable previous retrospective analyses of the impacts of the Waxman-Hatch Act include two by Henry Grabowski joint with John Vernon, Sr., a 1992 *Journal of Law and Economics* article, "Brand Loyalty, Entry, and Price Competition in Pharmaceuticals After the 1984 Drug Act", and a 1996 *PharmacoEconomics* article, "Longer Patents for Increased Generic Competition in the US: The Waxman-Hatch Act after One Decade".

The 1992 and 1996 Grabowski-Vernon analyses of the impacts of the Waxman-Hatch Act identified a number of very important issues and empirical findings, and have had a lasting and influential impact on subsequent research. For example, these classics characterized the typical pattern of generic entry and prices over the early years post-entry, the pricing responses by pioneers (and influenced a subsequent literature on brand loyalty and market segmentation), the resulting brand-generic market shares, highlighted distinctive paths taken by oral and injectable products, examined the role of manufacturer industry structure on the retail margins of generics and brands, and on the extent to which manufacturer price reductions flowed through to retail prices to cash-paying and third party payers.

An important empirical finding reported by Grabowski and Vernon [1992, 1996] was that, although other factors such as growth of managed care also had impacts on generic utilization, the Waxman-Hatch Act increased generic entry dramatically, intensifying price competition among generics

and resulting in brand pioneers losing market share much more rapidly and deeply than before 1984. In their 1996 summary, for example, they conclude: "The level of generic competition is very different one decade after, compared with before, the Act. In the early 1980s, the level of generic dispensing in the US was around 10%. By contrast, in the mid-1990s, the level of generic prescribing approached 40%."[1] Other provisions of Waxman-Hatch, however, had the effect of slightly extending effective patent life.

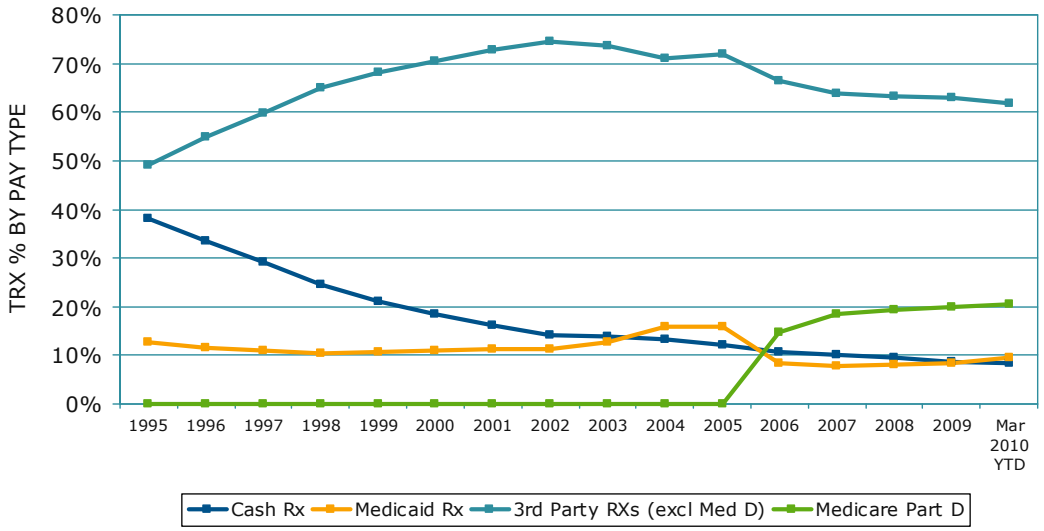
These findings on pioneer innovators' increased and more rapid loss of market share post-generic entry, offset to some extent by increased effective patent life, raised the issue of the net impact of the Waxman-Hatch Act on pioneer innovators' returns on R&D investments. In an influential study undertaken at the Congressional Budget Office, Anna Cook [1998] examined the present discounted value of the total stream of future profits expected from an average brand-name drug, after deducting costs of manufacturing, marketing, distribution, and other activities not related to R&D, before and after passage of the Waxman-Hatch Act. Cook acknowledged it would not be feasible to isolate the impact of the legislation, for other factors, such as repeal of state anti-substitution laws being replaced by state mandatory generic substitution provisions, and efforts by managed care to incent generic for brand substitution through use of tiered formularies with varying copayments, also likely had a non-trivial impact on generic entry and pricing pre- and post-1984. Cook concluded that although total discounted returns post-1984 were on average $27 million less in 1990 dollars than pre-1984, the combined effect of the various factors was modest: "For all drugs, on average, the increase in generic sales since 1984 has probably not reduced expected returns below the average capitalized costs of R&D. On the margin, however, it is possible that a few drugs that were barely profitable to develop before may no longer be so now."[2]

These classic and influential retrospective analyses of the impact of the Waxman-Hatch legislation were all based on data from the first decade following 1984 passage of the legislation. What trends have emerged since then? Has the nature of brand-generic and generic-generic competition changed, and if so, in what ways? With the benefit of a quarter century of data, what light can be shed on whether the "grand compromise" of Waxman-Hatch has struck the right balance between incentives to innovate and ensure access by consumers? While a number of other studies have been published in the intervening years, our differentiated focus here is to compare selected recent trends with those initially reported in the Grabowski-Vernon [1992, 1996] and Cook [1998] studies, and to identify other salient market developments.

Among the latter, three long-term developments that provide historical context for analyzing generic penetration are worth highlighting briefly. The first significant development is the growth of prescription drug insurance coverage. As seen in Figure 1, in 1995, a decade after implementation of Waxman-Hatch, about 38% of prescriptions were paid for by cash (without insurance), and 62% were covered by insurance (third party private 49%, and Medicaid 13%). Ten years later, in 2005 just before implementation of the Medicare Part D prescription drug benefit, the cash share of prescriptions had fallen to 12.1%, while 87.9% of dispensed prescriptions were covered by insurance, 71.9% by private third party payers, and 16.0% by Medicaid. In the first quarter of 2010, four years after implementation of the Medicare Part D benefit, the cash share had fallen to single digits – 8.3%, surpassed by Medicaid at 9.4%, Medicare Part D at 20.6%, and private third party payers, 61.7%. Whereas by one government

estimate the cash share of prescription drug spending share was 66% in 1980 and 55% in 1985[3], by 2010 the share of prescriptions paid for out-of-pocket had fallen to just 8%, and private plus public insurance covered 92% of dispensed prescriptions. To the extent competition among private prescription drug insurance plans involves providing consumers access to low cost drugs, we would expect greater drug insurance coverage to have placed increased demand on generic drug utilization and strong downward pressures on drug prices, particularly generic drugs.

FIGURE 1: DISPENSED PRESCRIPTION DRUG PAYMENT SHARES, 1995-2009
CASH, MEDICAID, MEDICARE PART D AND PRIVATE THIRD PARTY PAYER



Source: IMS Health, National Prescription Audit, Mar 2010

A second major development concerns recent changes in the number and relative importance of "blockbuster" drugs. As discussed in Aitken, Berndt and Cutler [2008], when defined as branded drugs having in excess of $1 billion (in year 2000 deflated dollars) in U.S. annual sales, the number of blockbuster drugs increased steadily from six to 52 between 1997 and 2006, and then fell in 2007 to 48; our updated calculations reveal relative stability in this number for 2008-2009. Over the same time period, the share of total U.S. pharmaceutical sales accounted for by blockbusters increased from 12 to 42% between 1997-2006, fell to 38% in 2007, and has remained relatively stable since then. Hence, whether measured by numbers or dollar share of sales, as early cohorts of blockbusters have gone off-patent and experienced sharp drops in sales due to competition from generics, in recent years they have not been fully replaced by new cohorts of recently launched new drugs achieving blockbuster status.

The third major development involves the growth in importance of biologic human therapeutic products. While biologic products remain concentrated in a relatively small number of therapeutic areas, as noted by Trusheim, Aitken and Berndt [2010] they can now be found at least in small numbers

in nearly every therapeutic class. In the discussion below of developments in the last quarter century involving brand-generic completion we focus on small molecules, for as of this point in time, none of the biologics in the U.S. has faced competition similar to that typically experienced by branded small molecule manufacturers following loss of patent expiration and extensive generic competition. While we expect passage of the Patient Protection and Affordable Care Act of 2010, which establishes an abbreviated regulatory process for approval of "biosimilars", will lead to significant future changes, we do not address those issues here.

Our outline is as follows. In Section II we provide a discussion of changes in rates of generic penetration since passage of the Waxman-Hatch legislation. We decompose generic penetration into share accessible to generics and generic efficiency rate components, both overall and for selected therapeutic areas. In Section III we consider the impact of generic penetration on consumer prices. We document that the approach commonly cited in the popular media, as represented by a highly publicized series of reports by the American Association of Retired Persons, incorrectly focuses only on price growth of leading brands, ignoring larger changes in marketplace dynamics. We offer alternative estimates incorporating generic substitution and changing market shares. In Section IV we expand the analysis and report on changes over time in the daily cost of treatment in nine aggregate therapeutic classes following recent patent expiration and generic entry. In Section V we offer discussion and conclusions.

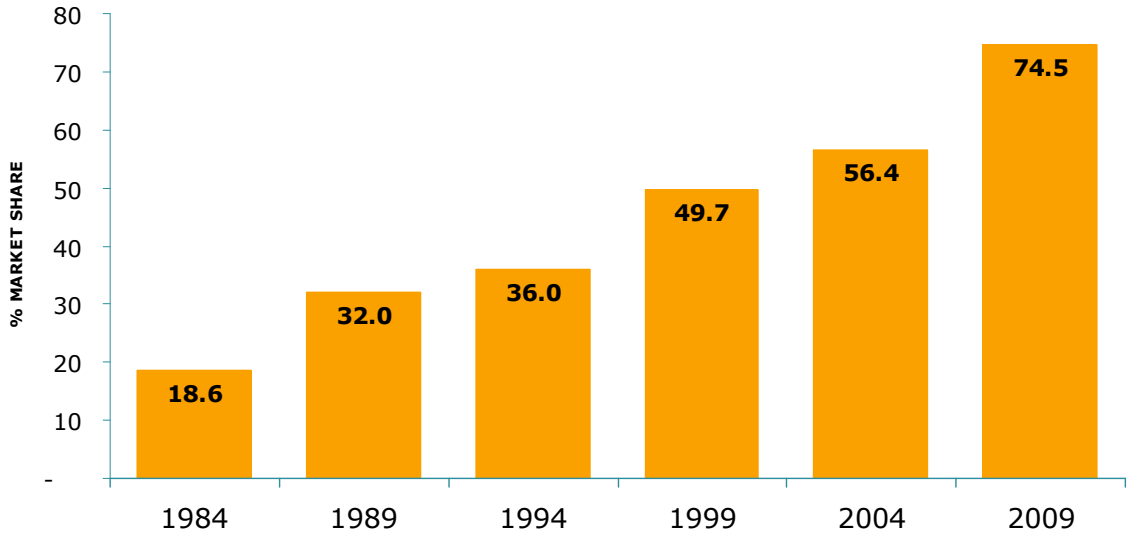
II . LONG-TERM AND RECENT TRENDS: GENERIC PENETRATION AND PRICES

Generic penetration can be measured in a number of different ways – share of extended units dispensed as generic (tablets, capsules, vials – earlier called countable units), and share of prescriptions dispensed as generic. The total generic share of prescriptions dispensed is by convention the sum of traditional unbranded generic and branded generic shares. Branded generics are defined by IMS Health as non-originator products that are either: (i) novel dosage forms of off-patent products; (ii) on patent with a trade name, but a molecule copy of an originator product; (iii) off-patent with a trade name; or (iv) off-patent without a trade name and from a single source or co-licensed.[4] IMS Health data separating out branded generic from unbranded generic prescriptions is only available beginning in 1998. We note in passing that in the future as "biosimilars" come to market, they will introduce an important new category of product that will make it more challenging to maintain clear brand-generic distinctions and interpret historical trends.

Figure 2 presents the trend in the generic and share of total prescriptions from 1984 to 2009, at five-year intervals. At the time of passage of the 1984 Waxman-Hatch Act, the generic share of prescriptions was 18.6%. A decade later in 1994, the generic share had almost doubled to 36%. After initially increasing sharply and then falling slightly (reflecting successful new branded product introductions in the mid-1990s), by 1999, fifteen years after passage of Waxman-Hatch, the generic prescription share was 49.7%, at almost 14 percentage points considerably greater than five years earlier. Between 1999 and 2004 the generic share increased modestly, by almost seven percentage points from 49.7% to 56.4%, but in the subsequent five years the generic share grew dramatically, by more than 18 percentage points, from 56.4% in 2004 to 74.5% in 2009. Hence, in very recent years

growth in generic share has accelerated substantially. Notably, this sharp acceleration in growth of generic share occurred not only as several important "blockbuster" branded drugs lost patent protection, but also during the time period in which the 2006 Medicare Part D benefit was implemented. We discuss Medicare Part D utilization of generic drugs in further detail in Section III below.

Figure 2: FIVE YEAR TRENDS in GENERIC SHARE OF TOTAL PRESCRIPTIONS, 1984-2009



Sources: For 1984-2004 IMS Health National Prescription Audit archives; for 2005-2009, IMS Health, National Sales Perspectives

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In summary, not only is the long-term trend in generic prescription shares an increasing one, it has also been accelerating recently, and is now increasing much more rapidly than what Grabowski and Vernon [1992, 1996] observed in the early years following passage of Waxman-Hatch. This acceleration raises a number of questions, such as: What are the factors underlying this rapid growth in generic prescription share? How much longer can the generic share continue to grow so rapidly? What are the factors potentially limiting growth in the generic prescription share?

A useful way to envisage changes underlying growth in the generic share is to view the latter as the product of two shares: (i) the market share accessible to generic substitution – generic volume plus brand volume for only those molecules for which generics are available in the time period of interest, divided by total prescriptions in the market (including brands for which no generic was available and generics for which no brand was available), multiplied by (ii) the generic efficiency rate – for only those molecules for which generics are available in the time period of interest, the share of generic volume in total brand plus generic volume. Results of this decomposition of generic (branded plus unbranded) market share growth since 2003 are presented in columns (1) – (3) of Table 2.

Both of the underlying components of the total generic market share have been increasing over the 2003-9 time period.. First, as the large number of brands approved in the "golden age" of the mid-1990s came off patent in the 2000s, and as fewer new molecular entities ("NMEs") mostly having smaller sales volume were launched, the market share of molecules susceptible to generics increased 16 percentage points from 65% in 2003 to 81% in 2009, approximately 2.5 percentage points a year, or on a proportional basis, by a cumulative 25%. Note that had manufacturers received FDA approval for a substantial number of new molecules that then achieved "blockbuster" status in the last decade, this market share susceptible to generic substitution could have declined even as older drugs went off patent. However, because of the relatively small number of NMEs approved by the FDA and the modest sales volumes they typically garnered, in fact this share susceptible to generic substitution has increased steadily. Second, due likely to a combination of greater proportion insured, formulary management, state mandatory generic substitution laws, and competition among private prescription drug plans offering low priced policies to Medicare Part D beneficiaries, the generic efficiency rate has also increased, from 77% in 2003 to 92% in 2009, 2.5 percentage points a year to a cumulative 15 percentage points, or on a proportional basis, by a cumulative 19%.

TABLE 2

DECOMPOSITION OF GROWTH IN GENERIC (BRANDED PLUS UNBRANDED) PRESCRIPTION SHARE AND REVENUE SHARE DISAGGREGATION, 2003-2009

	Prescriptions			*Revenue Dollars*		
	(1)	(2)	(3)	(4)	(5)	(6)
Year	Share Generic Accessible	Generic Efficiency Rate	Branded Plus Unbranded Generic Share	Unbranded Generic Share	Branded Generic Share	Branded Share
2003	64%	84%	54%	9.3%	7.6%	83.0%
2004	65	86	56	9.7	7.7	82.6
2005	67	90	60	10.1	8.8	81.1
2006	70	90	63	10.0	10.0	80.0
2007	74	91	67	10.8	10.0	79.2
2008	79	91	72	11.8	10.0	78.1
2009	81	92	74	12.5	10.6	76.9

Sources: Columns (1)-(3) IMS Health National Prescription Audit December 2009; columns (4)-(6) IMS National Sales Perspectives™ June 2010.

Since the generic efficiency rate is approaching its 100% ceiling, future growth in the total generic market share will depend critically on movements in the share generic accessible. With major brands among the statins, antidepressants, antipsychotics and proton pump inhibitors expected to lose

patent protection in the coming near future, it is reasonable to expect continued growth in the share generic accessible, and therefore in the total generic market share, albeit perhaps at slightly lower rates than in the recent past.

Variation in the roles played by the two components underlying total generic prescription share growth is particularly evident when looking across several distinct therapeutic classes. As seen in the top panel of Table 3, the calcium channel blockers class has attained very high rates of generic efficiency (almost 100%), so that when one leading brand (Norvasc™) began to face generic entrants in 2007, the

TABLE 3

TRENDS IN VARIOUS GENERIC PENETRATION RATES
SELECTED THERAPEUTIC CLASSES, 2004-2009

	2004	2005	2006	2007	2008	2009
Calcium Channel Blockers						
Market Share Generic Accessible	51%	51%	51%	84%	99%	100%
Generic Efficiency Rate	89	89	92	94	95	97
Generic Market Share	45	46	47	79	94	96
Lipid Regulators						
Market Share Generic Accessible	6%	7%	45%	46%	54%	60%
Generic Efficiency Rate	89	94	96	97	99	99
Generic Market Share	5	8	43	48	55	60
Anti-epileptics						
Market Share Generic Accessible	36%	54%	56%	57%	61%	81%
Generic Efficiency Rate	72	87	91	93	88	84
Generic Market Share	26	47	51	53	54	68

Source: IMS Health, National Sales Perspectives, National Prescription Audit

generic market share increased from 47% in 2006 to 96% in 2009. With no remaining protected calcium channel blockers currently in the market, this therapy area is now essentially entirely generic.

Another therapeutic area where the generic efficiency rate is almost 100% but generic market share has considerable future potential growth is the lipid regulators class. As seen in the middle panel of Table 3, when one leading brand (Zocor™) lost patent protection in 2006, the generic market share for the class increased from 8% in 2005 to 43% in 2006. Although the share of market accessible to generics was only 60% in 2006, when the current leading branded statin (Lipitor™) loses exclusivity as expected in 2001, one can expect a very substantial increase in both the share of market accessible by generics and the total generic market share for the lipid regulators. A rather different underlying dynamic is illustrated by anti-epileptic drugs, as shown in the bottom panel of Table 3. Generic efficiency rates in this therapeutic class have not been as high as with the lipid regulators and calcium channel blockers, but the share of market accessible by generics has increased dramatically, from 36% in 2004 to 81% in 2009, resulting in total generic market share growth from 26% in 2004 to 68% in 2009. The lower efficiency rate in this class may reflect clinical concerns among some prescribers, since retrospective claims analyses and case reports have associated generic substitution with well-controlled patients with epilepsy relapsing and experiencing breakthrough seizures.[5] Because the generic efficiency rate is only 84% for anti-epileptic drugs in 2009, there is further potential growth in the generic market share, but 100% efficiency may not be reached within this therapeutic class at this time. Additionally, IMS Health does not expect any additional major brands to lose patent protection in the next few years

TABLE 4

ANNUAL LEVELS AND GROWTH RATES OF RETAIL PRESCRIPTIONS DISPENSED AND EX-MANUFACTURER SALES REVENUES (CONSTANT $2000), 2003-2009

	Total Rx (billions)	Growth Rate (%)	Total Revenues (Billions $2000)	Growth Rate (%)
2000	3.034	6.5%	141.9	15.2%
2001	3.205	5.6	167.4	18.0
2002	3.301	3.0	187.9	12.2
2003	3.361	1.8	202.3	7.7
2004	3.435	2.2	214.5	6.1
2005	3.545	3.2	219.2	2.2
2006	3.706	4.5	232.0	5.8
2007	3.806	2.7	234.1	0.9
2008	3.846	1.0	233.5	-0.3
2009	3.922	2.1	242.7	4.0

Source: IMS Health, National Prescription Audit, IMS National Sales Perspectives June 2010

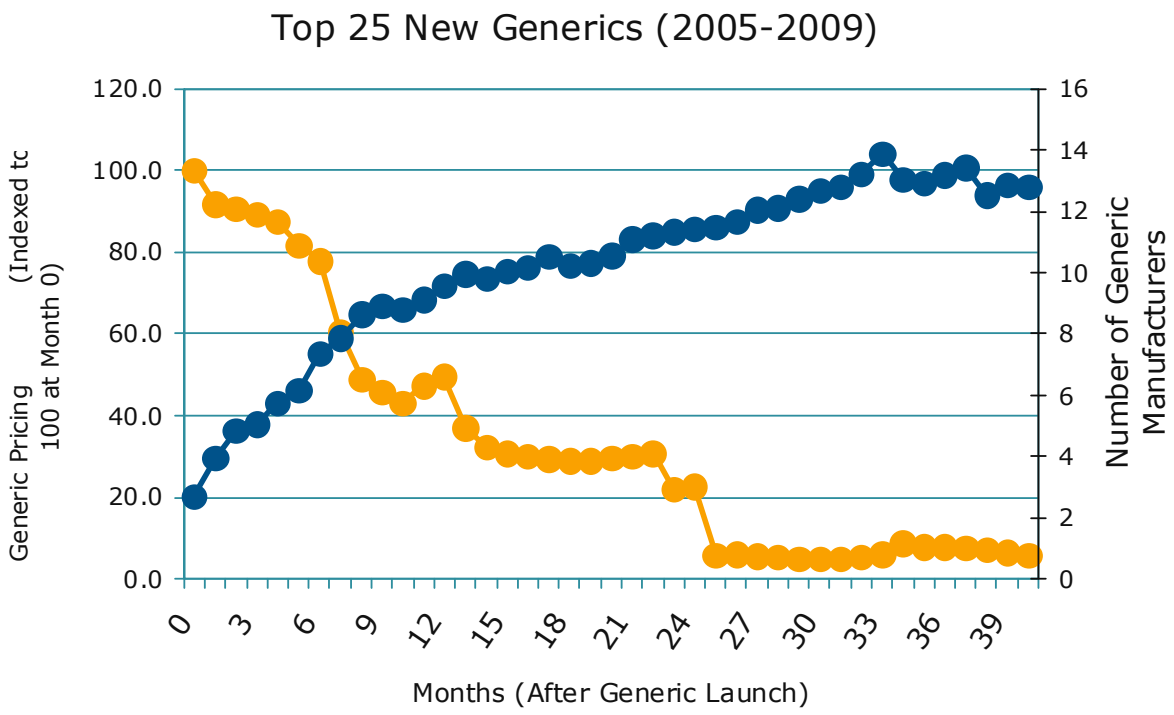
Before moving on to a discussion of generic price trends following passage of the Waxman-Hatch legislation, we digress briefly to assess the impact of rising generic use on changes in prescription drug spending. Annual 2000-9 levels and growth rates in the total number of retail (including mail order) prescriptions, and (constant year 2000) dollar ex-manufacturer revenues are given in Table 4. It is striking to note that duriing this decade, the number of prescriptions initially grew rapidly between 2000 and 2002, and then increased more slowly, averaging 2.5% annually, with a cumulative 2002-9 increase of about 19%. The slow growth in number of prescriptions was temporarily interrupted by the implementation of Medicare Part D in 2006, resulting in a growth rate of 4.5% that year. In contrast, since 2005 and particularly in 2007-9, inflation-adjusted revenues grew at very low rates relative to historical double-digit growth rates observed earlier in the 2000 decade, as has been noted by Aitken, Berndt and Cutler [2008]. This lower revenue growth rate towards the end of the decade reflects in part the substantial growth in the generic share of all prescriptions, which from Table 2 we see increased nine percentage points from 54% in 2003 to 63% in 2006, but then accelerated, increasing eleven percentage points to 74% in 2009. As noted elsewhere in a study undertaken by IMS Health, "For the decade 2000 through 2009, the use of generic prescription drugs in place of their brand-name counterparts saved the nation's health care system more than $824 billion dollars. In 2009 alone the use of FDA-approved generics saved $139.6 billion – a 15% growth over the prior year's savings – or about $382 million every day."[6]

In their 1996 study, Grabowski and Vernon reported significant generic price declines following initial generic launch, based on 1984-1991 data on the initial generic launches of 25 major molecules. They reported that after one year following initial generic entry, the average generic price index fell from 100 to 80, and after two years, to 65. To explore whether this trend has continued or accelerated in more recent years, in Figure 2 below we plot the monthly average generic price (indexed to 100 for the launch price of the first generic launched) and the number of generic entrants, with up to 40 months following initial generic launch on the horizontal axis, for the top 25 generic molecules launched between 2005 and 2009. Since not all generic molecules have been on the market for the full 40 quarters, for each month since launch the average is computed over the number of molecules having been on the market at least that length of time. The generic price index falls to a level of about 78 at month six, with an average number of generic entrants at seven. At months 12 and 24, the average generic price index falls to about 50 and 23, respectively, and then stabilizes at about 6 after month 25, even as the average number of generic manufacturers gradually increases to about 10, 11 and 12, respectively. Clearly, in the last five years rapid and extensive generic entry following initial loss of patent protection has led to correspondingly deep and rapid generic price declines.

Comparing the Grabowski-Vernon annual values to our monthly 2005-2009 initial generic launch prices in Figure 6 is not straightforward, given their differing periodicity. One reasonably simple way to approximate a one year generic price index using the 2005-2009 initial launch monthly data is to take the arithmetic mean of months 1-12, and for the two year generic price index, the arithmetic mean of months 13-24. This yields 2005-2009 one and two year price indexes of 68 and 28, respectively, which are much lower than the comparable annual 80 and 65 price index values based on 1984-1991 initial generic launches. Specifically, after one year the 2005-2009 launches have a price index 12 percentage

points (or on a proportional basis, 15%) lower than the 1984-1991 launches, and after two years, the 2005-2009 launches have a 37 percentage point (or, on a proportional basis, 57%) lower price index than the 1984-1991 launches. Thus the evidence clearly supports the hypothesis that generic price declines are much deeper and more rapid now than 25 years ago following initial implementation of the Waxman-Hatch legislation.[7]

FIGURE 2
Average Generic Price and Number of Generic Manufacturers Following Initial Generic Entry



Source: IMS Health, National Sales Perspectives, National Prescription Audit, Dec 2009

One other major development involving brand-generic substitution more generally is the emergence of intermolecular (not just intramolecular) substitution following a brand's loss of patent protection. A very notable, consistent finding and conventional wisdom until recently was that unit sales of the molecule (over its brand and generic formulations) typically fall following patent expiration.

For the first time in recent history, however, this conventional wisdom has been overturned by the cholesterol-lowering statin drugs. As reported in Aitken, Berndt and Cutler [2008], following limited generic authorized generic entry in the first six months following Zocor's™ loss of patent expiration[8], unfettered generic entry occurred in late December 2006. Since brand-name Lipitor™ was still patent-

protected in early 2007, whereas less costly generic versions of Pravachol™ (pravastatin) and Zocor™ (simvastatin) were now on the market, payers, insurers and PBMs were highly incented to switch patients on Lipitor™ to pravastatin or simvastatin. This typically took the form of moving Lipitor™ to the highest copayment tier, and placing the two generics on the lowest tier. For Pravachol™ and generic pravastatin, the total brand plus generic number of prescriptions since loss of patent protection increased only slightly. After Zocor™ lost patent protection, however, total monthly Zocor™ plus generic simvastatin prescriptions increased dramatically, from 2.8 million in June 2006 to 4.8 million in December 2007. A substantial portion of the new simvastatin sales came directly from previous Lipitor™ users or from patients who would have begun statin treatment with Lipitor™. In 2007, the number of prescriptions of Lipitor™ fell 12%, including 26% in new starts, and domestic sales of Lipitor™ measured in dollars fell 6.5% below 2006 levels. As best we can tell, the Lipitor™-simvastatin experience is the first major product instance in which generic versions of one molecule have substituted so significantly for brand-name versions of a different molecule; it certainly was not observed in the various Grabowsk-Vernon or Cook studies. Note that were such intermolecular substitution to become more common in the future, the impact would be to reduce not only the branded manufacturer's revenues whose innovator drug lost patent protection, but would also affect other branded manufacturers whose branded drug is therapeutically substitutable with the molecule now off-patent.

We return to a discussion of recent trends in prescription prices more broadly within a therapeutic class following generic entry in Section IV below.

III. DRUG PRICES - ACCOUNTING FOR CHANGING SHARES AND GENERICS

A much publicized and highly cited analyses of changes in drug prices has been a series of reports published over the last decade, coauthored by Leigh Purvis and Stephen Schondelmeyer for the American Association of Retired Persons ("AARP").[9] This series of reports, together with others focused on changes in brand prices, have contributed to the widespread perception that drug costs are "out of control". The headlines from these studies typically focus on the brand price index growth, e.g., "Brand Name Drug Prices Continue to Climb Despite Low General Inflation Rate", which is then contrasted with trends in generic prices, e.g., "In contrast, average manufacturer prices for widely used generic drugs fell during the same time period."[10] Some reports in the series, including one of the most recent, are devoted exclusively to brand price increases.[11] These reports have generated significant media attention and are frequently cited by policymakers. But do they address the relevant issue, and is the methodology they employ appropriate?

Using 2006 sales as fixed expenditure weights, the AARP authors construct an aggregate brand price index, an aggregate generic price index, an aggregate specialty price index, and an aggregate combined price index (over the leading 219 brands, 185 leading generics and 144 leading specialty drug products, based on number of prescriptions dispensed to Medicare Part D beneficiaries), annually for 2006 to 2009. In appendices, they also identify the top 25 brand, 25 generic and 25 specialty drug form-strengths (ranked by payment to manufacturer) The majority of the reports in the series use wholesale acquisition cost ("WAC") data, which AARP characterizes as the "manufacturer's price", to measure price per prescription, but beginning in August 2010, the series began using retail prices based on claims

data.[12] The AARP reports suffer from a number of conceptual and methodological flaws. Most problematic is the use of fixed 2006 expenditure weights for Medicare Part D beneficiaries, which results in the AARP price indexes failing to reflect the impact of generic entry for branded products coming off patent after 2006, as well as any other changes in the mix of drugs (whether brand or generic) used by Medicare patients over the 2006-2009 time period.[13] Moreover, even in the combined brand-generic price index reported in the May 2010 AARP report (Purvis and Schondelmeyer [2010]), brand and generic versions of the same molecule are treated as separate distinct products rather than as bioequivalent, thereby generating a well-documented upward bias in their aggregate price index calculations. [14]

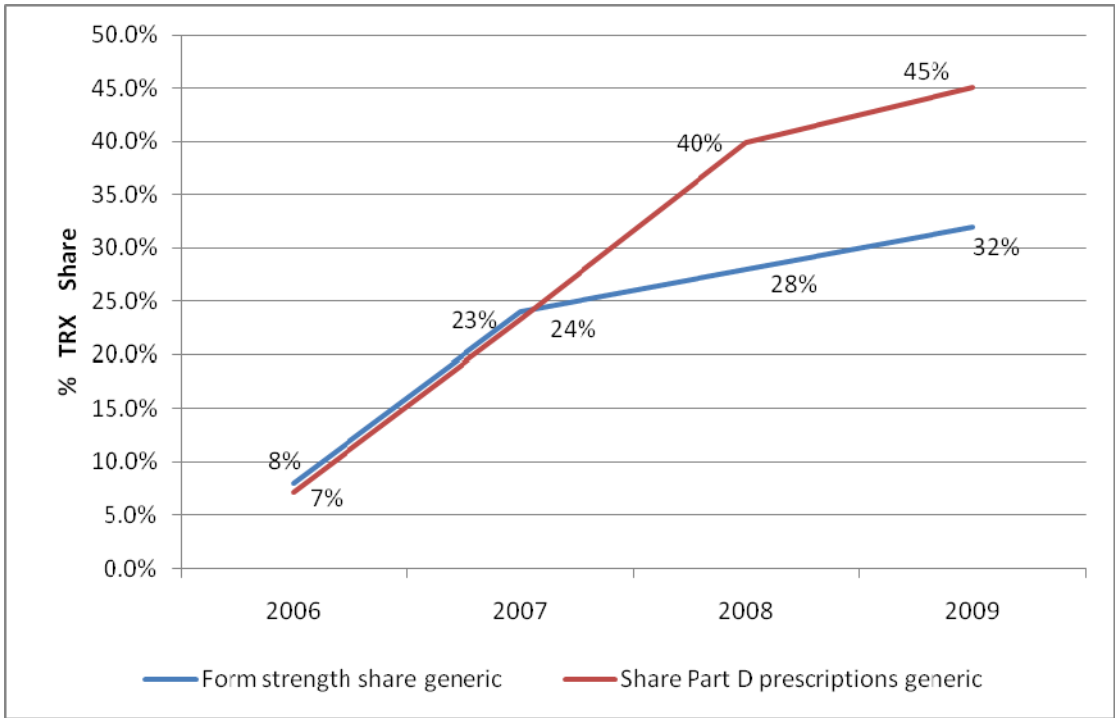
Regarding this latter point, already in 1995, fifteen years ago, the U.S. Bureau of Labor Statistics recognized the bias in its prescription drug Consumer Price Index ("CPI-Rx") induced by failing to link prices of newly entering lower priced generic drugs bioequivalent to higher priced branded molecules losing patent protection, and implemented procedures that explicitly linked these price decreases realized by consumers as they switched from brand to generic drug. Analogous links between prices of the same molecule branded and generic products in the BLS's Producer Price Index ("PPI-Rx") were implemented in January 1996.[15] The AARP study authors have not implemented such changes, and thus their reported price indexes suffer from an upwards bias. The magnitude of this upward bias depends on the extent of new generic entry and generic utilization, and on the relative price paths of brands and generics over time following patent expiration.

To gain information on the extent of the upward bias in these two 2010 AARP aggregate brand price index studies, we take the same 25 leading brand form-strengths identified by AARP, utilize their WAC list prices (while recognizing that use of actual transactions prices would be preferable), but for those brands going off patent, we link generic prices to their predecessor brand products by treating brand and generic versions of the same form-strength as bioequivalent (consistent with procedures adopted by the Bureau of Labor Statistics CPI-Rx and PPI-Rx programs in 1995-6), and allow for changing annual weights as brand-generic and other compositional changes have occurred since 2006. We derive IMS Medicare Part D prescription data from the IMS PlanTrak data base; as of January 2010, the IMS payer/plan universe contained 4,622 Medicare Part D benefit level plans.[16] For those brand form-strengths experiencing generic entry during 2006-9, brand and generic prescriptions are tracked separately, and then aggregated, with brand, generic and combined weights changing annually.[17] Rather than employing a fixed 2006 lens as is done in the AARP studies, this alternative methodology more accurately captures and portrays the dynamics of a rapidly changing pharmaceutical marketplace between 2006 and 2009, particularly with the dramatic changes brought about by the implementation of the Medicare Part D benefit in January 2006.

In this context, it is useful to note that by the end of 2009, nine of the 25 leading form-strengths identified by AARP had faced competition from generic entry (but Plavix™ only temporarily in 2006-7). Three of these had limited generic competition already in 2006 (Zocor™ in 20 mg and 40 mg form-strengths, and Plavix™ 75 mg – an at risk generic entry, subsequently ordered withdrawn), four form-strengths experienced initial generic entry in 2007 (Ambien™ 10 mg, Norvasc™ in 5 mg and 10 mg strengths, and Protonix™ 40 mg), and one faced initial generic entry in 2008 (Fosamax™ 70 mg) and in 2009 (Prevacid™ 30 mg). Figure 3 documents the extent of generic entry between 2006 and 2009,

measured alternatively by the share of the leading 25 brand form-strengths experiencing generic entry, and by the share of total leading 25 form-strength prescriptions dispensed to Medicare Part D beneficiaries as generics. Generic entry has been extensive with the share of form-strengths facing generic competition increasing four-fold from 8% in 2006 to 32% in 2009. Moreover, in part because of the growth in uptake by Medicare Part D beneficiaries over time and the aggressive generic penetration achieved by the prescription drug plans administering Medicare Part D benefits, the share of total brand plus generic prescriptions dispensed as generic for these leading 25 form-strengths to Medicare Part D beneficiaries increased more than six-fold, from 7.2% in 2006 to 45.1% in 2009. By 2009, almost half of the leading 25 form-strength prescriptions were dispensed as generics to Medicare Part D beneficiaries.

FIGURE 3: SHARE GENERIC NUMBER AND UTILIZATION OF FORM-STRENGTH DRUGS



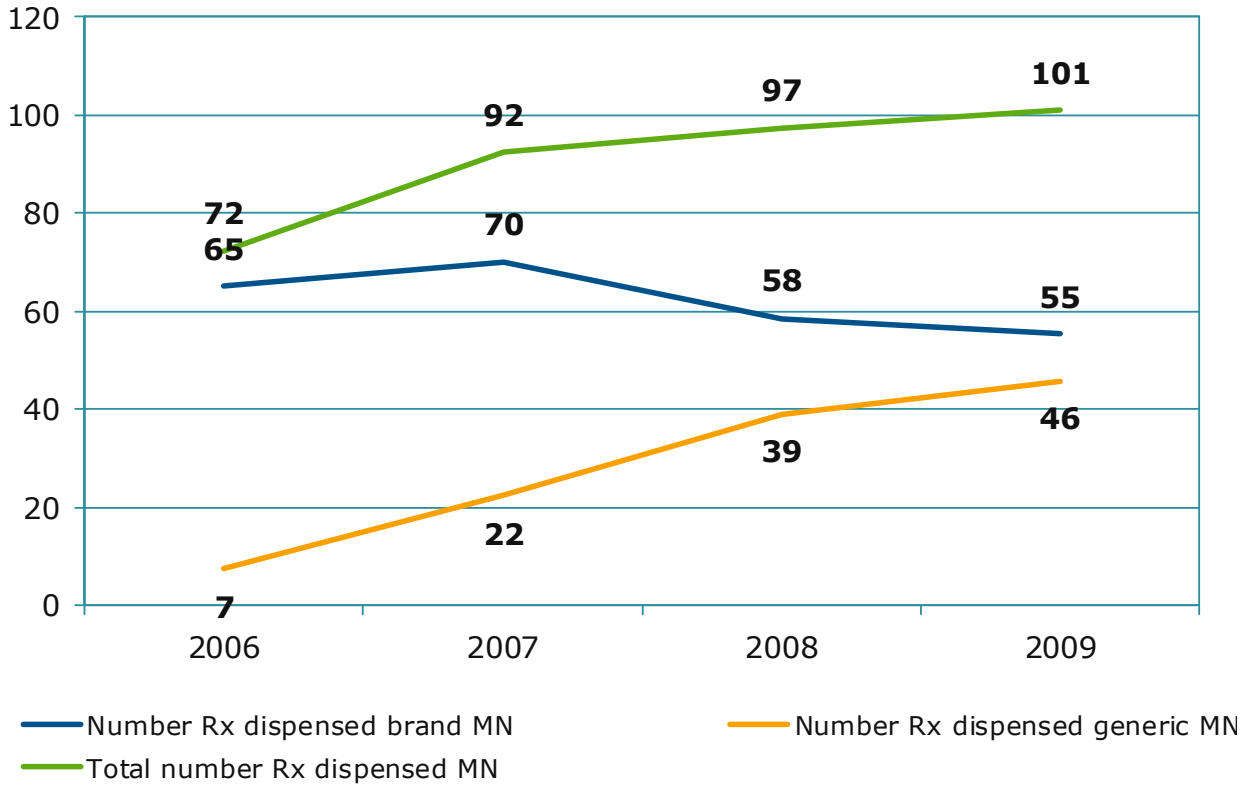
Source: IMS Plantrak, Medicare Part D dispensed prescriptions for the top 25 product-form-strengths in 2006

Figure 4 portrays the dramatically different experiences of brands and generics among these leading 25 form-strengths. Medicare Part D has indeed increased access to these medicines – the total number of prescriptions dispensed for these 25 form-strengths increased from 72 million in 2006 to 101 million in 2009 (an average annual growth rate of 11.8%), but this overall growth is entirely due to increased generic penetration. Specifically, while the number of top 25 form-strength prescriptions dispensed to Part D beneficiaries as brands fell from 65 million in 2006 to 55 million in 2009 (an annual average change of -5.3%), the number dispensed as generics rose dramatically, from 7 million in 2006 to 46 million in 2009, an annual average growth of 84.7%.

With almost half of all the Medicare Part D prescriptions in the sample of 25 leading selling drugs dispensed in generic form (and with almost three-quarters of all Part D prescriptions now dispensed as generics), one would reasonably expect that average prices facing Medicare Part D

beneficiaries through their private prescription drug plans fell substantially, making the Part D benefits more valuable to plan participants. These price declines are entirely overlooked by analyses that focus solely on brands, such as the AARP reports, which paint an ever less accurate picture of the Medicare Part D marketplace dynamics. Note, however, that in the current context in which we, like the AARP study authors, use the WAC list price rather than either manufacturers', retailers' or consumers' actual transactions prices, these price calculations are best interpreted as only approximating wholesalers' and retail chains' purchase prices from manufacturers, with the generic price trends being particularly problematic.

FIGURE 4: NUMBER OF TOTAL, BRAND AND GENERIC FORM-STRENGTH RX's DISPENSED



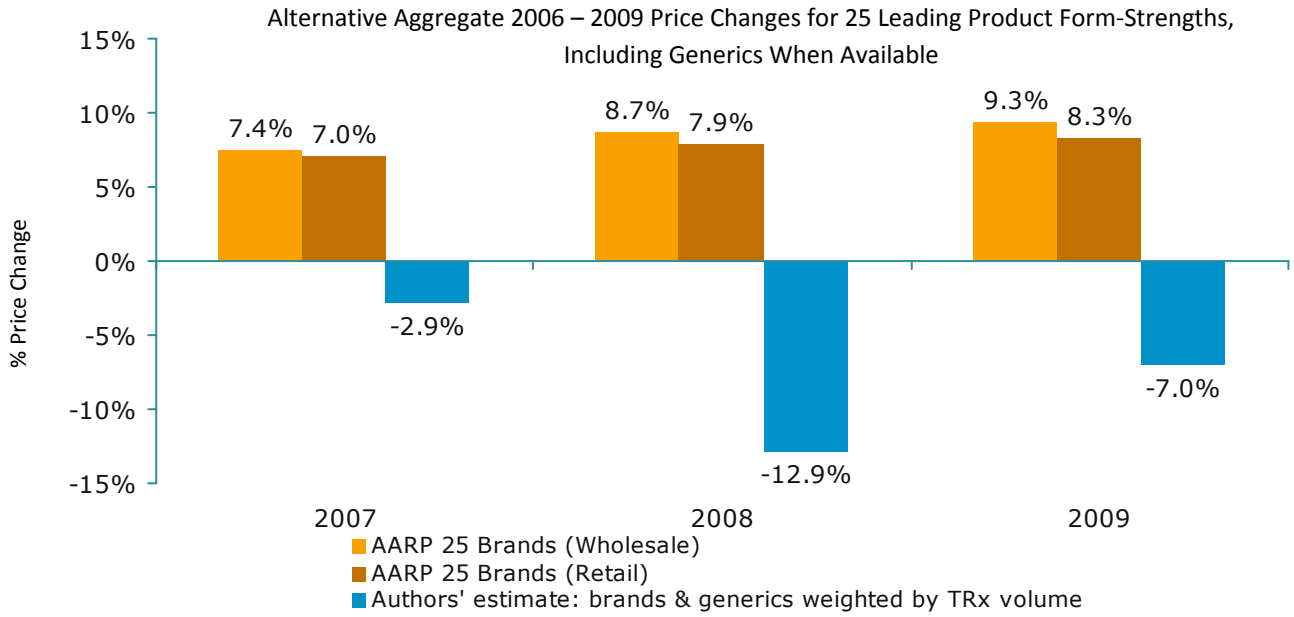
Source: IMS Plantrak, Medicare Part D dispensed prescriptions for the top 25 product-form-strengths in 2006

Although utilization of price index procedures as carried out by the U.S. Bureau of Labor Statistics is clearly preferable and represents best practice aggregate price measurement procedures, the simplest manner by which initially to depict the overall impact of market developments involving the leading selling 25 form-strengths identified by AARP is, for each year between 2006 and 2009, to divide

total revenues received by brand and generic manufacturers involving these 25 form-strengths (assuming average price received by manufacturers was equal to WAC, as was assumed in the AARP reports) by the total number of prescriptions dispensed, yielding an average overall price per prescription. As we shall discuss, this initial measure has a number of problems, but it is simple and easily understood, and we will augment it with price indexes computed by more preferable procedures.

Figure 5 indicates that between 2006 and 2009, the overall average price per prescription *declined* by 21.3%, a compounded average yearly change of -7.7% -- with 2007, 2008 and 2009 price *declines* of -2.9%, -12.9% and -7.0%, respectively. Over the same time period, because they both completely ignore generic entry as brands lost patent protection, the AARP studies report very different, incomplete and distorted price growth. For their price index based on manufacturer WAC prices ("AARP-W") they report a cumulative 2006-9 price *increase* of 27.6%, which corresponds to an average annual price *increase* of 8.5% -- with 2007, 2008 and 2009 price *increases* being 7.4%, 8.7% and 9.3%, respectively; for their aggregate price index based on retail claims data ("AARP-R"), they report a slightly smaller cumulative price *increase* of 25.0%, with 2007, 2008 and 2009 price *increases* being 7.0%, 7.9% and 8.3%, respectively.[18] The reason for the overall price per prescription decline in our more complete analysis is that any increases in brand prices have been more than offset by the marketplace dramatically shifting to lower priced generics – shifts that are entirely ignored in the two AARP studies. The shift to generics underlying the overall price declines likely reflects increased access by seniors to prescription drug benefits brought about by Medicare Part D, growth in market buying power of the Part D private prescription drug plans, and competition among chain pharmacies and mass merchandisers, such as WalMart offering 30 day prescriptions for numerous generic drugs for $4, and 90 day prescriptions for $10.[19]

FIGURE 5



Source: IMS DDD prices at WAC Level and IMS Plantrak Medicare Part D prescriptions, Dec 2009. AARP Rx Watchdog Reports (May 2010 & August 2010)

In this context, it is illuminating to document just how extraordinary has been the shift by Medicare Part D consumers to generics as brands lose patent protection, and how massive has the loss of market share by brands become when bioequivalent generic versions of the same form-strength became available, relative to what Grabowski and Vernon reported based on the early post-Waxman Hatch experience. Consider, for example, the three first form-strengths experiencing generic entry: Ambien™ 10 mg (initial generic entry in 2007), and the 40 mg and 20 mg formulations of Zocor™ (initial generic entry in 2006). In 2009, the brand shares in total brand plus generic prescriptions dispensed for these three form-strengths to Medicare Part D beneficiaries were 1.25%, 0.14% and 0.17%, respectively, implying that the manufacturers of these products lost 98.75%, 99.86% and 99.83% of their prescription market share between 2006 and 2009.[20] The Medicare Part D marketplace response in substituting to generic versions has been so strong in recent years that the resulting impact of brands' price increases on Part D participants' budgets is miniscule. By focusing only on brands and their price increases, the AARP price calculations and perspective entirely ignore these dominating market place developments.

One well-known problem with this simple overall average price per prescription set of calculations reported in the previous paragraphs is that it confounds changes in the price of a fixed basket of prescription form-strengths with changes over time in the share mix of products within the market basket. Hence, in the price index calculations we report below, consistent with professional best practice procedures, to portray the dynamic marketplace more accurately, we update weights annually (analogous to Bureau of Economic Analysis practices), and like the Bureau of Labor Statistics, we treat branded and bioequivalent generic products within the same form-strength as identical and bioequivalent (i.e., as perfect substitutes). By comparison, in both their 2010 studies the AARP authors employ a fixed weight (Laspeyres) methodology using 2006 fixed weights, and limit their analysis solely to brand name form-strength products, even when the brand is subject to FDA-designated bioequivalent same molecule generic competition. As best we can determine, the AARP methodology is unique unto itself. As we shall see, use of 2006 fixed weights when analyzing aggregate price trends through 2009 is particularly problematic, for as we have seen earlier, generic for brand substitution trends have been large and accelerating in recent years.

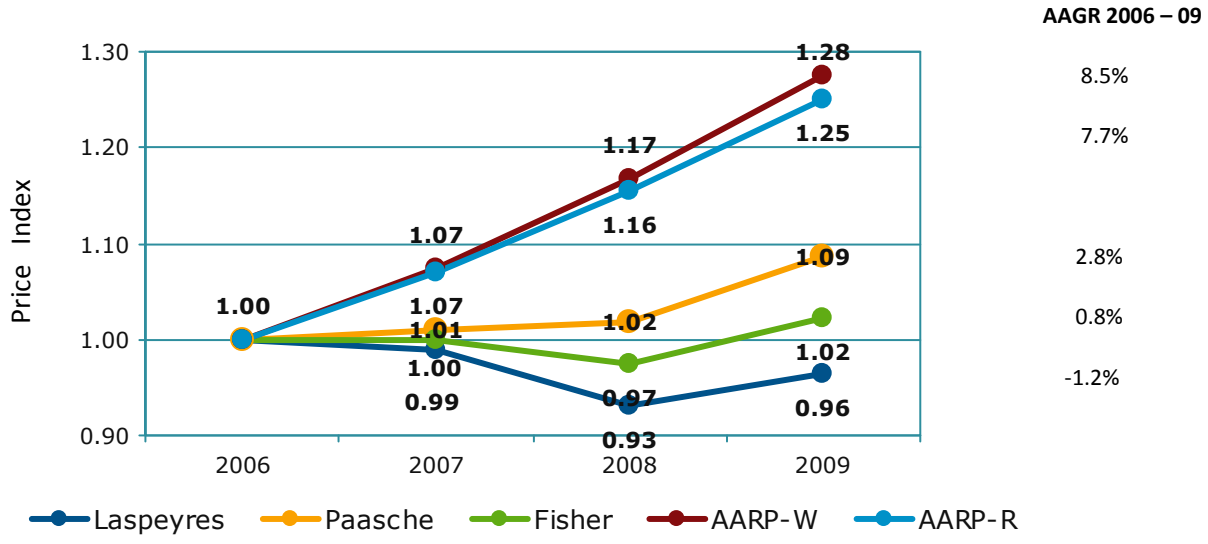
The construction and publication of price indexes based on professional best practice typically is based on one or more of three common alternative aggregate price indexes that differ depending on how they weight the price relatives – the price of a given product in period 1 divided by its price in period 0. If the price relatives are weighted by their time 0 ("base period") expenditure shares, the resulting price index is known as the aggregate Laspeyres price index; when the price relatives are weighted by their time 1 ("current period") expenditure shares, the resulting price index is known as the aggregate Paasche price index. Since it is unclear *a priori* whether using base period or current periodweights is preferable, many blend the two. The Fisher price index is simply the square root (also called the geometric mean) of the Laspeyres and Paasche price indexes; because it is a blend, it is frequently called the "Fisher ideal" price index.

When there are more than two time periods, one can maintain the time 0 expenditure weights in all future time periods (called fixed base weight indexes), or one can continually and sequentially update them, so that in say, time period 2 the "base period" weights are those of time 1 (not time 0),

and the "current period" weights are those of time 2 (not time 1); when sequentially updated in this manner the indexes are called chained price indexes. Currently the U.S. Bureau of Economic Analysis uses the chained Fisher price index when computing quarterly real gross domestic product and implicit price deflators, whereas when measuring monthly inflation the U.S. Bureau of Labor Statistics ("BLS") publishes a Laspeyres fixed weight price index, although the BLS updates the fixed weights every five to seven years. In the various price index results reported below, we employ chained weight price index procedures.

As seen in Figure 6, based on the "blended" Fisher price index formula (the green line), prices for the 25 form-strengths have increased 2.3% between 2006 and 2009, implying an average annual growth rate ("AAGR") of 0.8%. This blended index formula, utilized by the Bureau of Economic Analysis, reflects the net impact of differing trends when price relatives are weighted by base year (Laspeyres) or current year (Paasche) expenditure weights. Specifically, whereas the Laspeyres aggregate price index (purple line, at bottom) reveals a very slight decrease of 3.6% between 2006 and 2009 (an AAGR of -1.2%), the Paasche (orange line) generates an aggregate three year price increase of 8.6% (an AAGR of

.FIGURE 6: ALTERNATIVE AGGREGATE PRICE INDEXES (2006 = 1.000)
LEADING 25 MEDICARE PART D BRAND FORM-STRENGTHS AS OF 2006



Source: Authors' calculations

Note to Figure 6: The Laspeyres, Paasche and Fisher price index calculations are based on the WAC prices of the 25 leading form-strength products identified in the AARP branded samples. AARP-W and AARP-R are price indexes based on wholesale and retail prices, reported in Purvis-Schondelmeyer [2010] and Schondelmeyer-Purvis [2010], respectively.

2.8%). The reason the Laspeyres and Paasche generate different price trends involves the fact that in these data the expenditure shares of the various brand and generic form-strengths move very substantially between years, thereby weighting the price relatives differentially, i.e., the same price changes are weighted differently depending on which time period's shares are used as weights. Specifically, for those form-strengths having generic entry, expenditure shares are falling rapidly, and so use of lagged weights (Laspeyres) gives greater weight to the price declines than does use of the smaller current period (Paasche) weights. Other things equal, when shares are not changing as rapidly and as massively as is the case here, the various index number formulae typically yield results that are more similar to each other. The sensitivity of these aggregate price indexes to choice of base period, current period or blended periods highlights the inaccurate and distorted price index trends one obtains when one instead employs the fixed 2000 expenditure weights, as is done by the authors of the AARP studies.

However, in the current context, regardless of which of these three aggregate price index formulae is employed, the conclusion based on including both brands and generics in the sample consistently differs decisively from that reached by the AARP authors, whose AARP-W (blue) and AARP-R (purple) price indexes at the top of Figure 10 both increase much more rapidly than the various price indexes including both brands and generics (bottom three lines). In their wholesale price AARP-W calculations, the cumulative 2006-2009 price increase for widely used brand name prescription drugs was 27.6%, implying an AAGR of 8.5%, whereas in their retail price AARP-R calculations, the cumulative 2006-2009 corresponding price increase was 25.0%, implying an AAGR of 7.7%.[21] Clearly, relative to all the other price index measures, the AARP estimates are outliers and are upward biased estimates of price developments in the leading-25 form-strengths molecules.

IV. AVERAGE DAILY COST OF TREATMENT BY MAJOR THERAPEUTIC AREA

The construction of aggregate price indexes encompassing brands, branded generics and generics is one way in which the effects of brand-generic and other compositional changes can be documented. A more general approach involves quantifying changes over time in average pharmaceutical treatment cost per day for entire major therapeutic areas in which there have been both new product introductions and generic entry following patent expiration. Even more generally, rather than focusing just on pharmaceutical costs, one could compute total medical (and even non-medical) costs of treating an episode of an illness, as has been advocated elsewhere.[22] Here we summarize changes over time in pharmaceutical costs of treatment across nine major therapeutic areas that in 2005 accounted for about 25% of U.S. dollar sales and 18% of U.S. total prescription extended units and, and that have subsequently experienced initial generic entry at least once since 2006.

For each of nine major therapeutic areas, we compute average daily cost of therapy as follows: At each form-strength level, we multiply cost per extended unit (e.g., tablet, capsule, vial, etc.) times extended unit consumption per day times extended unit share of class, and then sum this up over all form-strengths of all products in the particular USC therapeutic class. Cost per extended unit is based on ex-manufacturer transactions into the wholesale and retail trade channels, projected to national totals. This calculation is done on a monthly basis just prior to generic entry, and with a focus on 12 months and 24 months post-generic entry. The nine therapeutic classes are (with their USC

classification code; their brand or brands going off patent; and date of initial generic entry): ace inhibitors (31110; Altace™; ramipril entry December 2007); antinauseants (17310; Zofran™; ondansetron entry December 2006); bisphosphonates (59210; Fosamax™; alendronate sodium entry January 2008); proton pump inhibitors (23420; Protonix™; pantroprazole entry December 2007); lipid regulators (32110 plus Vytorin™ and Zetia™; Zocor™ simvastatin entry June 2006); alpha-beta blockers (31410 plus 31420; Coreg™; carvedilol entry September 2007); antidepressants (64340; Zoloft™; sertraline entry June 2006)[23]; non-barbiturates and others (67290; Ambien™; zolpidem tartrate entry April 2007), and calcium channel blockers (31300; Norvasc™; amlodipine besylate entry March 2007). Results are presented in Table 5.

TABLE 5

AVERAGE DAILY COST OF TREATMENT ACROSS MAJOR THERAPY AREAS PRE-GENERIC ENTRY AND 12 AND 24 MONTHS POST GENERIC ENTRY

	Average Daily Cost			*Percent Reduction*	
Class	Pre-Generic	12 Months Post	24 Months Post	12 Months	24 Months
Antinauseants	$59.73	$25.69	$14.93	57.0%	75.0%
Bisphosphonates	2.01	1.35	0.32	32.7	84.1
Proton Pump Inhibitors	3.15	2.99	2.90	5.1	7.8
Lipid Regulators	2.52	2.13	1.86	15.3	26.2
Alpha-Beta Blockers	2.45	0.60	0.49	75.5	80.1
Antidepressants	1.60	1.03	1.06	35.8	33.8
Ace Inhibitors	0.49	0.37	0.27	24.0	43.9
Non-barbiturate, others	2.33	1.32	1.24	43.5	46.9
Calcium Channel Blockers	1.20	0.67	0.57	44.8	52.7

Source: IMS Health

At 12 months post-generic entry, the percent reduction in average daily cost of treatment among the major therapy areas ranges from 5.1% for the proton pump inhibitors to 75.5% for the alpha-beta blockers; the unweighted mean is 37.1%, and the weighted (by number extended units) mean is 27.5%. At 24 months post-generic entry, the percent reduction across major therapy areas in average daily treatment cost ranges from 7.8% for proton pump inhibitors to 84.1% for the bisphosphonates[24]; the unweighted mean reduction is 50.1%, while the weighted mean reduction is 35.1%. Note that this percent reduction is for the entire set of molecules in the therapeutic class following initial recent patent expirations, not for just that molecule going off-patent. As is seen in Table 5, these reductions in average daily costs following loss of patent protection are substantial, and in a number of cases, very large. We can expect that comparable savings in these and other classes will be realized in the next few years as well, as patents on major brands expire and generic entry occurs. Specifically, IMS Health reports that Flomax™ lost patent protection in April 2010 and it expects Aricept™ to face generic

entrants by November 2010. Market exclusivity is also expected to be lost in 2011 by Advair Diskus™ (September) as well as Lipitor™ and Plavix™ (November).[25]

V. DISCUSSION AND CONCLUSIONS

What have been the net effects of the "grand compromise" – maintaining a balance between ensuring finite patent protection to innovators and simultaneously providing access to lower cost generics following patent expiration -- in the last decade for consumers and manufacturers? Many of the initial trends identified by Grabowski and Vernon [1992, 1996] as having taken place in the first decade following implementation of the 1984 Waxman-Hatch Act have not only continued, but have intensified and occurred more rapidly in the last fifteen years. In particular, in recent years generic entry has been extensive, and consumer costs have declined dramatically.

Our analysis documents that for prescription drugs most commonly used by beneficiaries in Medicare Part D, the overall average price per prescription declined by 21.3% from 2006 to 2009, rather than increasing as reported by the AARP. By entirely ignoring generic entry and changing market shares, the AARP methodology generates a distorted and inaccurate portrait of the dynamics experienced by Medicare Part D beneficiaries and manufacturers of prescription drugs. Specifically, our analysis documents that any price increases by off-patent brands have been more than offset by massive shifts to generics.

A more comprehensive approach to measuring the effect of brand-generic and other compositional changes is to quantify changes over time in the average cost of biopharmaceutical treatment within various therapeutic areas. Our analysis finds that in each of nine major therapy areas average pharmaceutical treatment costs have declined, in some cases very dramatically (in one therapeutic class, 84.1%) following generic entry. These cost declines encompass the entire set of molecules within each therapeutic class, not simply the molecule whose patent has expired. Across all nine therapeutic areas, at 24 months post-generic entry, the weighted mean reduction in pharmaceutical treatment cost is 35.1%.

These declines in cost have had particularly significant impacts for Medicare Part D beneficiaries, and for the public sector funding of the Medicare Part D benefit. Indeed, the massive uptake of generic drugs by Medicare Part D beneficiaries has been one of the major contributors to actual Medicare Part D expenditures by the federal government in 2009 being only $60.8 billion, or 45% less than the $111.2 billion projected five years ago, shortly after the legislation was enacted.[26]

What do recent trends imply concerning the likelihood of achieving the right balance between innovators and consumers in the coming decade? In this year, 2011 and 2012, six of the ten leading selling products will encounter loss of market exclusivity, and a substantial number of branded franchises will be essentially eliminated. Updating the Cook [1998] Congressional Budget Office study to take into account numerous developments involving changes in brand loyalty, generic entry, price competition and regulatory oversight over the last fifteen years, along with their impacts on rates of return on biopharmaceutical R&D, would constitute a useful contribution to informing current and likely

future policy controversies. Looking beyond small molecules, it will be important to asses the longer term effects of the Patient Protection and Affordable Care Act of 2010 on entry and pricing of biosimilars, and on striking an appropriate balance between access to therapies and incentives for innovation (including supplemental indications)? More generally, there are many facets of the post-launch product life cycle, identified and quantified by Henry Grabowski's and his collaborators' research, on which we have not been able to devote attention here. Among those meriting updated and more detailed investigation are the effects of paragraph IV challenges and authorized generic entry[27], the impacts of more rapid and extensive loss of market share post-patent expiration, the appearance of significant cross-molecule substitution as brands lose patent protection, implementation of greater post-marketing requirements and risk evaluation and mitigation strategy commitments, increases in FDA submission user fees, and the relative lack of successful recent "blockbuster" drug launches, on the present values of R&D achieved by pioneer biopharmaceutical manufacturers over the last fifteen years, as well as changes in effective patent life. Comparisons across small molecule pharmaceuticals, biologics and vaccines are also of considerable importance to public and private sector decision-makers,[28] as are comparisons of biopharmaceuticals with medical devices.

The "grand compromise" of the 1984 Waxman-Hatch Act sought to maintain a balance between promoting and rewarding innovation while providing lower cost options following a finite patent protection period. As best we know, no other branded consumer market experiences such a dramatic predictable elimination of its brand franchise as does prescription biopharmaceuticals – even though the unchanged branded product remains safe and effective. In the last quarter century since passage of the Waxman-Hatch legislation we have witnessed a prototypical biopharmaceutical product life cycle with rapidly changing market dynamics, providing both manufacturers and consumers with benefits and challenges as the Schumpeterian process of "creative destruction" endures. [29]

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ENDNOTES

[1] Grabowski and Vernon [1996], p. 121.

[2] Cook [1998], p. xv.

[3] Department of Health and Human Services, April 2000, as reported in Berndt [2001], Exhibit 3, p. 104.

[4] In the IMS Health classification scheme, an example of (i) is Concerta™, an extended release formulation of methylphenidate hydrochloride, the active ingredient in the off-patent drug Ritalin™ used to treat attention deficit hyperactivity disorder, while the opiod analgesic Oxycontin™ is an example of (iii).

[5] See, for example, LeLorier, Duh, Paradis et al. [2008] and Crawford, Feely, Guberman and Kramer [2006].

[6] Generic Pharmaceutical Association [2010], p. 1.

[7] Comparison of number of manufacturers with the Grabowski-Vernon [1996] number of generic suppliers is not meaningful, since some manufacturers sell to repackaging generic suppliers.

[8] For a discussion and analysis of authorized generic entry, see Federal Trade Commission [2009] and Berndt, Mortimer, Bhattacharjya et al. [2007].

[9] Purvis and Schondelmeyer [2010] and Schondelmeyer and Purvis [2010]; also see Schondelmeyer, Purvis and Gross [2009a,b] and Gross, Schondelmeyer and Purvis [2008]. These and related reports in this series are available online at http://www.aarp.org/ppi.

[10] Purvis and Schondelmeyer [2010], p. 1.

[11] Schondelmeyer-Purvis [2010].

[12] Prior to August 2010, the AARP reports used the wholesale acquisition ("WAC") price published by Medi-Span as a measure of price per prescription. It is worth noting that the manufacturers' WAC price has no stable reliable relationship to prices paid by Medicare Part D beneficiaries for prescriptions dispensed at their pharmacies, for the latter include the effects of wholesaler, distributor, prescription drug plan and retail margins, as well as Medicare Part D subsidies to the prescriptions drug plans; for further details, see Berndt and Newhouse [2010]. Moreover, as pointed out by one of these authors previously, for generic drugs there is generally no stable or consistent relationship between the generic manufacturer's WAC and the acquisition costs of wholesalers and retail chains; see, for example, Schondelmeyer and Wrobel [2004, pp. 14, 17-18]. Despite these interpretive problems, he AARP authors have designated

this as the "manufacturer's" price. In their second 2010 study (Schondelmeyer and Purvis [2010]), the coauthors change the source of their pricing data from manufacturer to retailer, using prescription drug claims data from large medical claims data bases (Thomson Reuters MarketScan™ Commercial and Medicare Supplemental Research Databases).

[13] Notably, this use of fixed weights (along with the utilization of the fixed weight Laspeyres price index formula) represents a departure in methodology from Schondelmeyer's previous research published in peer-reviewed journals; see, for example, Suh, Schondelmeyer, Manning et al. [1998], in which changing weight Laspeyres, Paasche and Fisher aggregate price index procedures are employed.

[14]There are several other problems with the AARP methodology, and while not as egregious as the practice of ignoring generics, using list rather than transactions prices, and keeping 2006 expenditure weights fixed, they are worth noting. First, while the AARP WAC price is for a hypothetical prescription, say a pack of 30 tablets/capsules each taken once daily, manufacturers frequently sell wholesalers presentations containing a much larger numbers of tablets/capsules – bottles of 100, 500 or even 1000. Whether AARP uses a 30-day pack or a 1000 bottle formulation to compute a 30-day price for a medicine taken once daily is important, for typically the per tablet/capsule price is considerably smaller for the 1000 per bottle than with the 30 day pack presentation. Analogous issues arise for medicines taken once weekly, or several times per day. The AARP authors do not address the issue of how this biases upward their expenditure and price calculations. Second, as more prescriptions are dispensed for 90 days, it becomes increasingly important to measure the length of a prescription, rather than assuming it based on pack sizes. In the case of a package of 4 mg Avandia, for example, according to IMS data, the average number of pills in a prescription was 43.6, suggesting a significant number of patients had larger prescriptions than the pack size of 30 assumed in the AARP report. Ignoring consumers' shift to mail order and the increased share of 90 day prescriptions at retail pharmacies are each likely to understate the savings achieved by consumers, or alternatively, will bias upward estimates of price increases realized by consumers. Finally, although the set of brands "widely used by Medicare beneficiaries" on which the AARP bases its price growth calculations includes 219 form-strengths, AARP only publishes annual data for the leading 25 form-strengths.

[15] For discussion of this issue and references, see Berndt, Cutler, Frank et al. [2000], especially pp. 150-3 and 158.

[16] For further details concerning PlanTrak, see http://www.imshealth.com/portal/site/imshealth/menuitem.a46c6d4df3db4b3d88f611019418c22a/?vgnextoid=0c20362d14b73210VgnVCM100000ed152ca2RCRD&cpsextcurrchannel=1

[17] Since clopidogrel (the generic version of Plavix) was launched at risk by Canadian generic manufacturer Apotex, and then ordered withdrawn from the market shortly thereafter by Judge Sidney Stein, it never achieved a dominant portion of the clopidogrel plus Plavix market, and thus in the calculations reported here we treat all brand plus clopidogrel prescriptions as

branded throughout the 2006-9 time period. Notably, since the generic clopidogrel price was about 87% that of the brand, quantitative findings change only very slightly, and all qualitative findings are robust to how one treats those clopidogrel sales. For details on the Apotex entry and judicial decisions, see Aaron Smith [2007].

[18] Note that the average price growth over these leading 25 form-strengths is not strictly comparable to the AARP reported brand price growth, for the latter are based on 219 "widely used" brands; the AARP document does not report an average price growth for the leading 25 branded form-strengths, although it does identify the 25 products.

[19] See, for example, "$4 Prescriptions Program", available online at http://www.walmart.com/cp/4-Prescriptions-Program/546834, last accessed March, 21, 2010.

[20] Specifically, only about 62,000 of the 4.9 million zolipidem plus Ambien prescriptions were dispensed in brand form in 2009, while for simvastatin 20 mg plus Zocor 20 only 14,000 of 8.3 million prescriptions were dispensed as brands, and for simvastatin 40 mg plus Zocor 40 mg only 13,000 of 9.6 million were dispensed as brands.

[21] Schondelmeyer, Purvis and Gross [2009a], p.1; the 2009 value was annualized during the 12 months ending in September 2009, but is the same as that reported in Purvis and Schondelmeyer [2010], p. 1. Over the same 2006-9 time period, the corresponding AARP aggregate price index over the combined product sample consisting of 219 brand products, 185 generics and 144 specialty products increased 14.2%, an AAGR of 4.53%.

[22] See, for example, Berndt, Cutler, Frank et al. [2000].

[23] Although Effexor (venlaxafine) went off patent in June 2008, we do not report 24 months beyond that date here.

[24] We note that the proton pump inhibitors class is one where the availability of over-the-counter therapeutic options is widespread and may be partially responsible for the relatively low level of reduction in average prescription-only treatment cost following the introduction of generic prescription-only pantoprazole.

[25] We note that BMS has applied for a six month pediatric exclusivity extension for Plavix™. If this application is approved by the FDA, the date at which Plavix™ would lose market exclusivity would move to mid-2012.

[26] Dinan [2010].

[27] For a discussion of Paragraph IV challenges and authorized generics, see Berndt, Mortimer, Bhattacharjya et al. [2007], and Federal Trade Commission [2009].

[28] Such research would build on the recent comparison of the post-launch experiences of small molecules and biologics by Trusheim, Aitken and Berndt [2010].

[29] For a discussion of the roles of patent protection and innovation in benefiting consumers over the longer term – the "Schumpeterian hypothesis" and the critical role of "creative destruction" – see, for example, Scherer and Ross [1990], pp. 613-60.