Introduction

Thirty years ago, Congress sought to create a balance between access to lower cost generic medicines and incentives to innovate new and better medicines by passing the Drug Price Competition and Patent Term Restoration Act (the Hatch-Waxman Act) of 1984. This balance has now been in place for three decades and has delivered public health and economic benefits far greater than ever could have been imagined when the law was enacted.

Today, 86 percent of all prescription medicines dispensed in the United States are generic – a staggering figure. More than 90 percent of approved drugs have generic versions available and millions of patients across the country rely on them to provide safe, affordable choices to improve their health. As we celebrate the 30th anniversary of the Hatch-Waxman Act, this milestone offers the opportunity to both reflect on the true impact of the law over the past 30 years, and to look forward to the future of further growth, innovation and progress for affordable medicines.

A Look Back: Making Generic Drugs Available to the American People

In 1938 Congress passed the Federal Food, Drug, and Cosmetic Act (FDCA) in response to the deadly elixir sulfanilamide incident. This law designated drugs introduced after 1938 as “new drugs” requiring studies to show safety. The FDCA was amended in 1962 to require new drugs manufacturers to prove efficacy as well as safety. More importantly, this amendment allowed for the approval of generic versions of brand name drugs approved prior to 1962 via a “paper” New Drug Application (NDA).

The “paper” NDA process was woefully underused. Only 15 of the 150 drugs that were off-patent had approved generic alternatives in 1980. This would not, however, be the case for very long. In 1984 – after months of deliberations and debate among members of Congress and fierce negotiations between competing drug industry trade associations – the Hatch-Waxman Act was signed into law by President Ronald Reagan on September 24, amending the FDCA to create a generic approval pathway via an Abbreviated New Drug Application (ANDA).

In the first year following the enactment of the Hatch-Waxman Act and the establishment of the ANDA approval pathway, the Food and Drug Administration (FDA) received approximately 1,050 ANDAs. By the end of the second year, the substitution rate for FDA-approved generic drugs had increased from 12 percent to 22 percent. The generic substitution rate continued to increase each year, reaching 42 percent, 50 percent, and nearly 66 percent 10 years, 20 years,
and 25 years, respectively, following the passage of the Hatch-Waxman Act. By 2014, the
generic substitution rate climbed to an astounding **86 percent**. Increased generic substitution
has directly resulted in increased savings to both consumers and the U.S. health care system
(see graph below).

_Savings for Patients and the U.S. Health Care System_

According to a 2014 analysis by the IMS Institute for Healthcare Informatics, over the 10-year period 2004 through 2013, generic drug use generated nearly $1.5 trillion in savings to the U.S. health care system. In 2013 alone, generics saved $239 billion. ²

Generic versions of brand name drugs provide consumers with affordable alternatives to prescribed medicines. A 2012 report from the National Association of Chain Drug Stores showed that the average retail price for a generic prescription was $35.22, while the average retail price for a brand-name prescription was $121.18, a difference of more than 70 percent.³

The Centers for Medicare and Medicaid Services (CMS) issued findings in January 2014 that showed slower growth in health spending resulted from “all-time high savings” from the use of

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1 Annual generic utilization and savings data compiled from IMS Health, the Generic Pharmaceutical Association, and the Congressional Budget Office.
2 Annual generic utilization and savings data compiled from IMS Health, the Generic Pharmaceutical Association, and the Congressional Budget Office.
generic medicines. CMS reported that retail prescription drug spending slowed “as the result increased sales of lower-cost generics.”

Beyond substantial savings, generic medicines also increase patient adherence to prescribing orders, which improves health outcomes. A July 2009 study “Medication Adherence and Use of Generic Drug Therapies,” conducted by the American Journal of Managed Care, showed that prescribing lower cost generics was associated with improved adherence. This is important because the high cost of drugs is a common reason patients decide not to take medications, even though proper medication adherence can add years to a patient’s life. The American Heart Association reported in July 2013 that, “Poor medication adherence takes the lives of 125,000 Americans annually and costs the health care system nearly $300 billion a year in additional doctor visits, emergency department visits and hospitalizations.”

By any measure, the Hatch-Waxman Act has been a resounding success in achieving the goals of improving patient access to affordable medicines and providing savings to the health care system while promoting innovation of new branded pharmaceuticals. As a result, the United States both has the most successful generic drug market in the world and remains the world’s leader in new drug innovation. Against the prolific success of the Hatch-Waxman Act in enhancing public health, incentivizing new drug development, and providing system-wide economic sustainability, it is critical that we maintain this crucial balance as the next generation of new and innovative medicines enters the market.

The availability of low-cost generic alternatives has resulted in both economic benefits for consumers and public health contributions to the U.S. economy. In addition to the economic and public health benefits, the Hatch-Waxman Act also spurred new drug innovation.

**Spurring New Drug Innovation**

The competition in the pharmaceutical marketplace that generic medicines currently provides is an important part of the life cycle of a drug, both assuring affordable access to life-saving cures and spurring innovation and research into new cures. Even the best of medicines are of no value if their high cost puts them out of reach for patients who need them. The patent term restoration provision of the Hatch-Waxman Act, which lengthened patent terms for innovator drugs, provides the necessary incentives for brand manufacturers to develop new medicines.

According to data from the U.S. Patent and Trademark Office, new drug innovators have been granted more than 1,100 years in patent life extensions for their branded drugs since 1984

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4 Centers for Medicare and Medicaid Services. “National Health Spending Growth Remains Low for 4th Consecutive Year.” (January 2014)
when the patent term restoration provision of the Hatch-Waxman Act became law. That equates to more than 35 years of extra patent protection for each year the Hatch-Waxman Act has been in effect.\(^7\)

A Government Accountability Office report released in November 2006 found that the pharmaceutical industry’s “annual inflation-adjusted research and development expenses steadily increased from less than $16 billion to nearly $40 billion – a 147 percent increase” from 1993 through 2004.\(^8\) An October 2006 Congressional Budget Office (CBO) study showed that inflation adjusted spending on research and development (R&D) for new drugs grew between “three-fold and six-fold” during the first 25 years since the passage of the Hatch-Waxman law.\(^9\)

Another report showed that brand drug companies spent $65.2 billion in 2008 for the research and development of new drugs, and that since 2000 over $500 billion has been invested in R&D.\(^10\) Between 2004 and 2014, “more than 300 new medicines have been approved by the FDA, helping patients live longer, healthier lives. Medications are transforming many cancers into treatable conditions, reducing the impact of cardiovascular disease, offering new options for patients with hard-to-treat diseases like Alzheimer’s and Parkinson’s, and fighting even the rarest conditions.”\(^11\)

In 2013, “more than 5,000 medicines were in development globally, all of which have the potential to help patients in the U.S. and around the world. According to another data source, there are 3,400 medicines in development today just in the United States, an increase of 40 percent since 2005.”\(^12\)

The impact of the Hatch-Waxman Act is clear in one brand manufacturer’s response to looming generic entry into its marketplace. In the face of generic competition to its antidepressant Prozac, Eli Lilly responded by formulating an innovation strategy to develop a new-and-improved Prozac replacement three years

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\(^12\) Pharmaceutical Research and Manufacturers of America. “Explore the Drug Discovery Pipeline.” (2014)
before the drug’s patents expired. Lilly’s Prozac survival strategy was to “pour resources into
drug development to push four new drugs to market from late 2001 to early 2003 [the time of
Prozac generic market formation],” said Lilly President Sidney Taurel. Lilly’s vision was to
outgrow generic competition “through a constant stream of innovation.” Numerous other
examples abound that show competition drives innovation.

A Look Forward: Biosimilars – The Next Frontier

As science and medicine continue to evolve, the Hatch-Waxman Act provides a foundation for
improving access to complex biologic medicines that represent the largest part of today’s drug
development pipeline. Biologics are medicines that are derived from living cells and used to
treat many serious, often life-threatening, conditions. Biologics are far more structurally
complex than traditional chemical drugs, typically containing 200 to 1000 times the number of
atoms per molecule. Today, there are approximately 900 new biologics in development,
targeting more than 100 diseases. This translates into a big business: the global biologics
market is expected to soar to $220 billion by 2019, nearly double the current $120 billion
market.13

One of the reasons the market is so large is price – biologic medicines are costly. The annual
cost of a biologic can be several hundred thousand dollars.14 Research shows that the average
daily cost of a biologic product is approximately 22 times greater than the daily cost for a small
molecule drug.15 Data show that the prices of biologics continue to increase. Between 2011
and 2012, prices for specialty drugs – a category of drugs that includes biologics – increased by
12.9 percent.16

While biologics are often the only lifesaving treatments for the most severe diseases, their high
price tag can keep them out of reach for many patients. Fortunately, for the many patients who
benefit from biologic treatments and for those providing and paying for health care, there is an
answer. The approval of generic versions of expensive brand-name biologic medicines will
create the necessary competition in the biologic marketplace to significantly lower costs for
patients, providers, and to the whole health care system. Just as competition has reduced the
prices of traditional prescription drugs, it will create the market dynamics needed to lower the

publications.com/biologics-and-biosimilars-world-markets/
Affairs. 32(10): 1803 – 1810.
2009/12/03/kramer-health-care-intelligent-investing-pharmaceuticals.html
cost of biologics. The availability of more affordable biologic medicines will translate into enormous savings for patients, taxpayers, insurers, providers, and state and federal governments.

Despite the potential for increased competition and savings, prior to 2010, there was no regulatory approval pathway for generic versions of biologics in the United States.

In 2010, Congress passed the Biologics Price Competition and Innovation Act (BPCIA) as part of the Affordable Care Act (ACA) which established the regulatory approval pathway for generic versions of biologic drugs, known as biosimilars. The BPCIA is intended to bring competition to the biologics market in the same way that Hatch-Waxman brought competition to the small molecule drug market. The BPCIA also is intended to stimulate innovation and investment in the next generation of originator biologics and it is mutually beneficial if this happens alongside the availability of biosimilars.

In 2007, “biotechs accounted for 42 percent of preclinical candidates and 26 percent of submissions for US marketing approval.”\(^{17}\) Between April 2013 and March 2014, five of the top 12 selling drugs in the U.S. were biologics. By 2016, up to eight of the top 10 drugs on the market will be biologics.\(^{18}\)

Much like small molecule generic drugs, biosimilar competition is expected to be the most important opportunity to hold down the cost of biologic medicines and to spur the development of new, innovative biologics. A recent study found that an effective biosimilars pathway could save the U.S. health care system $250 billion over 10 years.\(^{19}\) This estimate was based on 11 existing biologics that are the most likely candidates for biosimilar competition in the next 10 years; the savings will grow significantly as more biologics lose patent protection and more biosimilars enter the market.

Over the next few years, the number of biosimilar medicines available to patients may grow dramatically. By 2020, brand biologic medicines worth an estimated $81 billion in global annual sales will lose their patents opening those markets for biosimilar alternatives (see table).20

**Brand Biologics Losing Patent Protection by 2020:**

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Active Substance</th>
<th>U.S. Expiry Date21</th>
<th>U.S. Sales Through March 201422</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neulasta®</td>
<td>Pegfilgrastim</td>
<td>2014</td>
<td>$3,634,919,067</td>
</tr>
<tr>
<td>Humira®</td>
<td>Adalimumab</td>
<td>2016</td>
<td>$5,936,288,498</td>
</tr>
<tr>
<td>Lucentis®</td>
<td>Ranibizumab</td>
<td>2016</td>
<td>$1,917,919,037</td>
</tr>
<tr>
<td>Rituxan®</td>
<td>Rituximab</td>
<td>2016</td>
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</tr>
<tr>
<td>Avastin®</td>
<td>Bevacizumab</td>
<td>2017</td>
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<tr>
<td>Remicade®</td>
<td>Infliximab</td>
<td>2018</td>
<td>$4,235,535,358</td>
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<tr>
<td>Herceptin®</td>
<td>Trastuzumab</td>
<td>2019</td>
<td>$1,971,724,243</td>
</tr>
</tbody>
</table>

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21 Source: IMS MIDAS, June 2013, IMS Patent focus.

22 Source: IMS National Prescription Audit, IMS Health. Data in this table reflects sales for the period April 2013 through March 2014.
Biosimilars now are available in 50 countries around the world. The demand for affordable biologic alternatives grows as governments cope with aging populations and an increase in chronic diseases. The use of safe and effective biosimilar therapies is a proven way of reducing health care costs while at the same time delivering lifesaving treatments to patients in need.

The European Medicines Agency (EMA), the European counterpart to the U.S. FDA, laid out a framework for developing and marketing biosimilars in 2004, and by 2006, it approved the first biosimilar and made it available for patients. Today, 19 biosimilar medicines are available to patients in the EU. Total sales of biosimilar medicines in the E.U. approached an estimated $500 million in 2014. Cost savings in Europe from biosimilars are estimated to be between $16 billion and $43 billion by 2020.23

As anticipated in the U.S., companies that want to make and market a biosimilar therapy in the EU are required to submit quality data and comparability data. The extent of this scientific process varies by medicine type and each biosimilar is evaluated on a case-by-case basis.

Although biosimilars are not yet available in the U.S., there is steady progress towards approval. In July of 2014, the FDA accepted the first application for approval of a biosimilar medicine, signaling the beginning of the FDA biosimilar review process. In August of 2014, the FDA accepted a filing for approval for a biosimilar monoclonal antibody – which signals a significant development because monoclonal antibodies are much more complex than most other biologic medicines. And, as of September 2014, pharmaceutical companies have requested more than 75 meetings with the FDA to discuss the approval process for biosimilars for 14 different biologics.

The FDA also published on September 9, 2014 the “Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations.” The Purple Book lists biological products, including any biosimilar and interchangeable biological products, licensed by FDA. The lists include the date a biological product was licensed under 351(a) of the Public Health Service (PHS) Act and whether FDA evaluated the biological product for reference product exclusivity under section 351(k)(7) of the PHS Act.

Despite this continued progress and the promising potential of biosimilars, manufacturers of brand biologics are hard at work to prevent competition from these medicines. Some brand biologic companies are particularly focused on convincing regulators that a biosimilar should not share the same International Nonproprietary Name (INN) as the reference biologic.

It is important to note that this notion of separate INNs for a biologic and its biosimilar counterpart was rejected by Congress during the many BPCIA debates. The legislation left to FDA the decision on how to designate the name of biosimilar products for purposes of doctors, pharmacists, patients and public health professionals prescribing and using the medicines. The decisions that the FDA makes about how to name these therapies will affect patient access, market competition, and global standards. The FDA currently is working on a guidance document to address biosimilar naming; the guidance is expected to be published by the end of 2014.

Conclusion

In the past 30 years, the generic drug industry has put lifesaving and life-changing medicines in reach for millions of Americans. The savings delivered each year are more than 200 times greater than predicted three decades ago, with $239 billion saved in 2013 alone.

The 30th anniversary of the Hatch-Waxman Act marks a pivotal point in the history of the pharmaceutical industry. Looking back, generics have a remarkable story of increased access and lowered costs. Looking forward, the future is bright as the industry embraces the emerging opportunities of a global marketplace, an aging population, record expansions in health coverage, and the next frontier of affordable medicines: biosimilars.