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Follow-On Biologics: Is The Incentive For Development Still Present?

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I. INTRODUCTION

Biologics are medical treatments and products originated from living organisms.¹ Biologics are an area of great advancement and give rise to several life saving therapies. It is estimated that approximately fifty percent of all drugs approved by the U.S. Food and Drug Administration (FDA) in 2010 will be biologics.² Biotech drugs are the fastest growing of our nation's prescription drug bill, as well as the most expensive.³

The Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, created an expedited process for generic pharmaceuticals to enter the marketplace.⁴ The Hatch-Waxman Act, however, does not cover most biologics and follow-up biologics were hindered by the lack of a regulatory process.⁵

On March 23, 2010, Congress enacted Patient Protection and Affordable Care Act (PPACA) with the aim of providing affordable health care coverage to a greater population.⁶ As part of the wide range of initiatives undertaken by PPACA, the legislation established a regulatory pathway in which the FDA can now approve generic "follow-on biologics" products.⁷

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1. Henry Grabowski, Iain Cockburn & Genia Long, *The Market for Follow-on Biologics: How Will It Evolve?*, 25 HEALTH AFF. 1291, 1291 (2006).

2. Press Release, U.S. House of Representatives Committee On Energy & Commerce, Bipartisan Group of Members Introduces "Promoting Innovation and Access to Life-Saving Medicines Act" (March 11, 2009), available at <http://democrats.energycommerce.house.gov/index.php?q=news/bipartisan-group-of-members-introduces-promoting-innovation-and-access-to-life-saving-medicines>.

3. *Id.*

4. See Grabowski et al., *supra* note 1, at 1292.

5. See *id.*

6. See Sherly Gay Solberg & Robert Pear, *Obama Signs Health Care Overhaul Bill, With a Flourish*, N.Y. TIMES, March 23, 2010, at A19.

7. See Patient Protection and Affordable Care Act (PPACA), H.R. 3590, 111th Cong. § 7002 (2009) (enacted).

The need for providing affordable health care must be balanced against providing incentives to innovators so they can recoup their investments of time, labor, and resources made in arriving at their invention.⁸ The PPACA grants the biotech firm that created the initial reference product a twelve-year exclusivity provision,⁹ which is longer than that afforded to pharmaceutical companies under Hatch-Waxman.¹⁰ However, there is a great debate as to whether this FDA exclusivity will erode the incentives already in place under traditional patent protections.¹¹

This article focuses on the regulatory scheme of biologics established in PPACA, using the Hatch-Waxman Act as a backdrop to assess the economic benefits to both the consumer and innovator. While high costs to consumers illustrate a need for generic alternatives to brand-name biologics, the prices incurred by innovators will most likely not be made up by the regulatory scheme and, thus, may stifle further innovation.

II. THE DRUG PRICE COMPETITION AND PATENT TERM RESTORATION ACT: THE HATCH-WAXMAN ACT

A. *The Substance of Hatch-Waxman*

Before the early 1980's, drug companies that sought to develop a generic of an already patented drug were required to wait until the statute of limitations ran on the patent before they could begin the FDA application process.¹² In response to the needs of the consumer and the concerns of the drug manufacturers, Congress enacted the Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman) in 1984.¹³ Hatch-Waxman established the Abbreviated New Drug Application (ANDA), a process that allows generic drug manufacturers to demonstrate bioequivalence between their generic and the FDA approved brand drug before the patent of the branded drug expires.¹⁴ Under

8. See Lydia Pallas Loren & Joseph Scott Miller, *Intellectual Property Law: Cases & Materials*, 111 (Semaphore Press, 2nd ed., 2010).

9. H.R. 3590 at § 7002 (enacted).

10. See Grabowski et al., *supra* note 1, at 1296.

11. Maxwell R. Morgan, *Regulation of Innovation Under Follow-On Biologics Legislation: FDA Exclusivity As An Efficient Incentive Mechanism*, 11 COLUM. SCI. & TECH. L. REV. 93, 97 (2010).

12. Sarah E. Eurek, *Hatch-Waxman Reform and Accelerated Market Entry of Generic Drugs: Is Faster Necessarily Better?*, 2003 DUKE L. & TECH. REV. 2 (Aug. 13, 19 (2003).

13. See *id.*

14. Martha M. Rumore, *The Hatch-Waxman Act-25 Years Later: Keeping the Pharmaceutical Scale Balanced*, PHARMACY TIMES, (Aug. 15, 2009), <http://www.pharmacytimes.com/supplement/pharmacy/2009/GenericSupplement0809/Generic-HatchWaxman-0809>.

ANDA, generic drug manufacturers are not required to repeat the clinical trials performed by the original innovator and patent holder.¹⁵ To establish bioequivalence, the generic drug manufacturer must demonstrate that their generic drug meets the same standards for strength, quality, purity, and identity as the branded product.¹⁶

To ensure that Hatch-Waxman did not forsake innovation while attempting to drive down the price of biologics, the bill also rewarded the technological advancements made by the drug manufacturers. The Act allowed for five-year data exclusivity for New Molecular Entities (NMEs).¹⁷ It also established a three-year exclusivity period for supplements requiring clinical trials.¹⁸ Moreover, there is a 180-day exclusivity period for the first ANDA granted.¹⁹ This allows for competitive pricing and provides a market share incentive for the first generic manufacturer against subsequent generic drugs.²⁰

B. The Effect of Hatch-Waxman on the Generic Drug Industry

Since the passing of Hatch-Waxman and its subsequent revisions, consumers have been afforded the ability to purchase generic alternatives to their prescription drugs. In 2000, the average cost per prescription for generic drugs was \$19.33, roughly \$50 less than their brand name counterpart.²¹

However, Hatch-Waxman seems to have had somewhat of a deleterious effect on the drug companies' incentive to invest in research and development. In the mid-1990s, the FDA approved approximately 120 new applications each year.²² In 2001, the FDA approved 66 new drug applications, nearly half of the previously approved applications.²³ One study concluded that consumers "lose roughly \$3 in health benefits due to future innovation for every \$1 gained due to easier access to generic drugs in the short term."²⁴ A decreased incentive to invest in research and development means less innovation in discovering new medication. With statistics like these, the consumer may win in the

15. Eureka, *supra* note 12, at 19.

16. *See id.*

17. Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 FOOD & DRUG L.J. 187, 188-89 (1999) (discussing the overview of Hatch-Waxman).

18. *Id.*

19. Rumore, *supra* note 14.

20. *Id.*

21. Eureka, *supra* note 12, at 2.

22. *Id.* at 12.

23. *Id.*

24. *Id.*

short term under these regulations, but the decrease in research and development indicate that both the consumer and drug companies will lose in the long term.

III. THE BIOLOGICS PRICE COMPETITION AND INNOVATION ACT OF 2009

A. *The Substance of the Biologics Price Competition and Innovation Act*

With the price of biologics increasing and several patents due to expire in the upcoming years, Congress and the FDA felt pressure to establish a regulatory scheme for a biosimilar “follow-on” biologics as such products were not covered by Hatch-Waxman.²⁵ For a product to be a follow-on biologic, the product must be similar or highly similar to the initial, reference biologic.²⁶

When the PPACA was signed into law on March 23, 2010,²⁷ Section 7002, the provision regulating the pathway for biosimilar biological products, went into effect immediately.²⁸ The Biologics Price Competition and Innovation Act (Biologics Act) establishes a regulatory process for licensing biosimilar follow-on biologics before the expiration of a patent.²⁹ The Biologics Act allows for a twelve year exclusivity to the original biologic (known as the reference product) from the date on which the product was first approved by the FDA.³⁰ No follow-on biologic company may file an application until four years from the date the reference product was first licensed.³¹

An application for a follow-on biologic to be biosimilar to the reference product must contain certain FDA certifications.³² To pass the certification, an applicant must show the product is biosimilar to the reference product by presenting analytical studies, animal studies, and data from a clinical study sufficient to demonstrate safety, purity, and potency.³³ The administration, dosage, and strength of the biological product must be the

25. Grabowski et al., *supra* note 1, at 1291.

26. BIOTECHNOLOGY INDUSTRY ORGANIZATION, *A Follow-on Biologics Regime Without Strong Data Exclusivity Will Stifle The Development of New Medicines*, 1, http://www.bio.org/healthcare/followonbkg/FOBSDData_exclusivity_20070926.pdf (last visited Apr. 22, 2011) [hereinafter BIOTECHNOLOGY INDUS. ORG.].

27. *See* Solberg & Pear, *supra* note 6.

28. *See* H.R. 3590 at § 7002 (enacted).

29. *See id.*

30. *Id.*

31. *Id.*

32. *Id.*

33. *See id.*

same as the reference biologic.³⁴ Yet, unlike generic drugs, a biological product can be biosimilar even if minor differences exist.³⁵ The standard of measurement for biosimilars is “highly similar,” and does not require the biologics to be identical.³⁶

B. The Cost of Development for Pharmaceutical Drugs Compared to Biologics

Biologics are currently responsible for over \$60 billion worth of sales in the U.S. drug market.³⁷ These drugs are growing at a rate twice that of chemical drugs.³⁸ While the sample of biologics studies is small in comparison to that of chemical drugs, the data suggests that the cost of research and development for biologics is about \$403 million per new drug.³⁹

A recent study also suggests that the development phase of new biologics requires higher manufacturing costs than for prescription drugs.⁴⁰ The cost of materials for biologics is higher due to the nature of the product.⁴¹ Particularly, cell cultivation requires considerable capital and is highly labor intensive.⁴² In 2002, the cost of materials for biologics ranged from 20-100 times than used for chemical drugs.⁴³ With the required investment of such massive amounts of time and capital, appropriate incentives must be in place in order to foster the innovation of biologics.

C. The Regulatory Scheme: Is There Enough Incentive?

The PPACA extends the exclusivity period for reference biologics to twelve years.⁴⁴ While strictly looking at the numbers, it would seem that the twelve-year exclusivity period would be sufficient to foster innovation as it is greater than the exclusivity period of traditional chemical drugs. Furthermore, advocates of the regulatory scheme suggested an even further limited period of data exclusivity. Representative Waxman and his co-sponsors suggested that the five-year exclusivity awarded to chemical drugs

34. H.R. 3590 at § 7002 (enacted).

35. *Id.*

36. *Id.*

37. *See* Grabowski et al., *supra* note 1, at 1291.

38. *Id.*

39. *Id.* at 1292-93.

40. *Id.* at 1293.

41. *Id.* at 1294.

42. *Id.*

43. *See* Grabowski et al., *supra* note 1, at 1294.

44. Morgan, *supra* note 11, at 99.

have created an increase in generic drug manufacturing and, therefore, should be applied to biologics.⁴⁵ However, looking at the twelve-year exclusivity period, in light of the costs associated with research and development of biologics, it is too early to tell whether the process that worked for regulating generic chemical drugs is the proper method for biologics.

As compared to the large pharmaceutical firms, the biotechnology industry is largely comprised of small, privately funded companies.⁴⁶ In 2005, out of the 1,415 biotechnology companies, only 329 were publicly traded.⁴⁷ These small companies experience a great deal of economic uncertainty, resulting from both the large amount of early capital needed to develop a drug candidate and lack of product revenue.⁴⁸ The cost of capital for a large pharmaceutical company is on average 15.7 percent, whereas the cost of capital for biotechnology companies with at least one drug approved is on average 18.7 percent.⁴⁹ For those biotechnology companies with only a drug candidate in clinical trials, the cost of capital averages 27.4 percent.⁵⁰

The biotechnology industry suggested a minimum of a fourteen-year exclusivity for biologics.⁵¹ In making that assessment, it analyzed the unique elements of the biotechnology industry.⁵² The studies and statistics have illustrated that the investment cost and technological complexities involved in developing biologics seems to grossly differ from that of prescription drugs.⁵³ As a result, the breakeven point for biologics is between 12.9 and 16.2 years.⁵⁴ That means under the current twelve-year exclusivity period, biologic manufacturers would not recoup their investment for their technology before the introduction of follow-on biologics.

Furthermore, evidence has shown that the introduction of generics in chemical drugs has decreased the number of new drug applications to the FDA.⁵⁵ If the cost of research

45. *Id.*

46. BIOTECHNOLOGY INDUS. ORG., *supra* note 26, at 5.

47. *Id.* at 6.

48. *Id.* at 5.

49. *Id.*

50. *Id.*

51. Morgan, *supra* note 11, at 99.

52. BIOTECHNOLOGY INDUS. ORG., *supra* note 26, at 5.

53. See Grabowski et al., *supra* note 1, at 1294.

54. BIOTECHNOLOGY INDUS. ORG., *supra* note 26, at 4.

55. See Eurek, *supra* note 12, at 12.

and development is greater for biologics than drugs, what is to say that this regulatory scheme will not have a similar, if not greater, deleterious effect on the growth of new biologics?

IV. CONCLUSION

Section 7002 of PPACA encompasses a great deal of new legislation aimed at providing the public with affordable, accessible healthcare. With the rising price and need of biologics, the demand for follow-on biologics is evident. Yet, there is a sizable cost of research and development associated with biologic innovation. The twelve-year exclusivity may not provide enough incentive to biologic manufacturers and could stifle future biologic research rather than spawn a new branch of follow-on generics. Consequently, while consumers will gain affordable biologics in the short term, in the long term, both the consumer and biotechnology industry may ultimately be hindered by the decrease in innovation.