

DEFINING LIMITS TO THE APPLICATION OF THE STATUTORY EXPERIMENTAL USE EXCEPTION WITHIN THE AGRICULTURAL BIOTECHNOLOGY INDUSTRY

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2015 MICH. ST. L. REV. 509

ABSTRACT

The Hatch–Waxman Act delineates a pathway for the approval of generic drugs by the Food and Drug Administration (FDA). In addition to an abbreviated generic drug approval process, the Hatch–Waxman Act added a new defense to patent infringement, a statutory experimental use exception. The statutory experimental use exception allows pharmaceutical companies to conduct research on patented technologies if the research might be used in a regulatory submission to the FDA.

In a separate article, I argued that the statutory experimental use exception should apply to the agricultural biotechnology industry's development of genetically engineered crops. Arguments were based on the Supreme Court's broad interpretation of the underlying statute and the FDA's regulation of genetically engineered (GE) crops. Such an application of the experimental use exception would have a potentially large impact on the patent valuations within the agricultural biotechnology industry.

This Article describes the limitations of the statutory experimental use exception of the Hatch–Waxman Act in light of the patent strategies employed by the agricultural biotechnology industry. Based on these limitations, this Article argues that intellectual property protection is still valuable to agricultural biotechnology companies if the statutory experimental use defense were available to the industry. Part I describes the development of the statutory experimental use exception and its evolution. Part II

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explains the intellectual property protection necessary for the agricultural biotechnology industry due to the regulations and long development timelines. Part III analyzes the case law surrounding the statutory experimental use exception in light of GE crop intellectual property protection to describe the reach of the statutory experimental use exception within the industry.

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INTRODUCTION

In 2012, E.I. DuPont De Nemours and Company (DuPont) and Pioneer Hi-Bred International, Inc. (Pioneer) attempted to invoke the Hatch–Waxman statutory experimental use exception defense against claims of patent infringement in litigation against Monsanto Company and Monsanto Technology, LLC (Monsanto).¹ The statutory experimental use exception exempts certain uses of patented inventions from infringement liability— specifically, uses in research conducted on inventions in order to gain approval by the

1. *Monsanto Co. & Monsanto Tech., LLC v. E.I. DuPont De Nemours & Pioneer Hi-Bred Int'l, Inc.*, No. 4:09-cv-00686-ERW (E.D. Mo. June 29, 2012) (PACER).

Food and Drug Administration (FDA).² The court in the *Monsanto* case refused to apply the defense to the agricultural biotechnology industry. As a result, instead of a judgment of noninfringement, Monsanto received a one-billion-dollar award based on Monsanto's evidence of the reasonable royalty it might have charged in order to conduct research using its patented technology.³

The one-billion-dollar award reflects the value of Monsanto-owned patents named in the suit. Monsanto is one of the largest agricultural biotechnology companies in the world; it develops and produces genetically engineered (GE) crops, among other products. As such, Monsanto relies on a variety of patents protecting all possible aspects of its products and development program. The high valuation on the patents for research alone should illustrate why Monsanto would be against the application of the statutory experimental use exception in the agricultural biotechnology industry. Monsanto likely—and rightly—fears that its patents would be less valuable if it could not enforce them against competitors conducting research on Monsanto inventions. Application of the statutory experimental use exception would limit patent infringement liability of competitors for such acts.

The Hatch–Waxman Act delineates a pathway for the approval of generic drugs by the FDA.⁴ In addition to an abbreviated generic drug approval process, the Hatch–Waxman Act added a new defense to patent infringement, a statutory experimental use exception. The statutory experimental use exception allows pharmaceutical companies to conduct research on patented technologies if the research might be used in a regulatory submission to the FDA.⁵

This Hatch–Waxman statutory experimental use exception has been expanded from its initial use in the development of generic drugs to include a variety of other uses in the pharmaceutical industry.⁶ In a separate article, I argue for the applicability of the

2. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, § 202(e)(1), 98 Stat. 1585, 1603 (codified as amended in scattered sections of 15, 21, 35, and 42 U.S.C.).

3. *Transcript of Record at 255*, Monsanto Co. & Monsanto Tech., LLC v. E.I. DuPont De Nemours & Pioneer Hi-Bred Int'l, Inc., No. 4:09-cv-00686-ERW (E.D. Mo. Aug. 16, 2012) (No. 1581), 2012 WL 8438518.

4. 35 U.S.C. § 271(e)(1) (2012). In 2003, Congress amended this scheme in Title XI of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, §§ 1101-18, 117 Stat. 2066, 2448-64 (codified at 21 U.S.C. § 355 (2012)).

5. 35 U.S.C. § 271(e)(1).

6. See *infra* Section I.B.

statutory experimental use exception to the agricultural biotechnology industry in light of that industry's reliance on patent protection for GE crops.⁷

This Article describes the limitations of the statutory experimental use exception of the Hatch–Waxman Act in light of the tri-agency regulatory scheme and the patent strategies employed by the agricultural biotechnology industry. Based on these limitations, this Article argues that intellectual property protection would still be valuable to agricultural biotechnology companies if the statutory experimental use defense were available to the industry. Part I describes the development of the statutory experimental use exception and its evolution. Part II explains the intellectual property protection necessary for the agricultural biotechnology industry due to the regulations and long development timelines. Part III analyzes the limitations on the applicability of the statutory experimental use exception based on intellectual property protection strategies and the multi-agency regulation approach to describe the reach of the statutory experimental use exception within the industry.

I. THE STATUTORY EXPERIMENTAL USE EXCEPTION

The statutory experimental use exception developed out of the gap left by the death of the common law experimental use exception and the need for better access to generic versions of drugs. Since its enactment, the application of the statutory experimental use exception has evolved to cover more than merely generic drugs. However, the coverage is not absolute.

A. Creation of a Statutory Experimental Use Exception

Well before the creation of the statutory experimental use exception, a common law experimental use exception arose and was abolished. As early as 1813, judges read the patent system to include a common law experimental use exception to infringement liability. The seminal case is that of *Whittemore v. Cutter*, in which Justice Story established the experimental use exception as a defense to patent infringement if the infringement occurred during the process

7. Jennifer Carter-Johnson, *Ritalin to Roundup: Expanding the Pharmaceutical Industry Statutory Experimental Use Exception to Agriculture*, U. CIN. L. REV. (forthcoming 2015) [hereinafter “Ritalin to RoundUp”].

of scientific research.⁸ This common law experimental use exception evolved to encompass uses in which the invention was not made for profit, including the use of a patented invention in order to improve it⁹ and to procure an improvement patent.¹⁰

Courts began limiting the common law experimental use exception in the late 1970s and early 1980s as the commercial interests of the patent owner became more important to the analysis. First fell the use of a patented invention to develop a new product in *Pitcairn v. United States*¹¹ and *Roche Products v. Bolar Pharmaceutical Co.* Then, the Federal Circuit held that any commercial purpose disallowed the common law experimental use exception even if no product developed from the research.¹² Finally, the Federal Circuit held that the non-profit or commercial status of an accused infringer did not matter as long as the infringing activity furthered a legitimate business interest.¹³

Interestingly, the *Roche* decision dealt with the development of generic drugs. In *Roche*, a generic drug manufacturer used a patented drug to perform experiments for submission to the FDA once the patents had expired.¹⁴ It was largely in response to the *Roche* decision that the Hatch–Waxman statutory experimental use exception developed.

As the application of the common law experimental use exception contracted, the healthcare industry evolved to comply with an increasingly complex regulatory structure. At the same time, consumers expected cheaper, non-patent protected, i.e., generic, versions of drugs to become available as patents on drugs expired.

Patent protection allows the patent owner the right to exclude others from using the product. In an industry with a long regulatory pathway, such as the pharmaceutical industry, this translates into delays in bringing generic drugs to the marketplace and thus an artificial extension of the patent term. Because patents prohibit new entrants into a product marketplace until after expiration, the

8. *Whittemore v. Cutter*, 29 F. Cas. 1120, 1120-23 (C.C.D. Mass. 1813) (No. 17,600).

9. *Swain v. Guild*, 21 F. Cas. 554, 555 (C.C.D. Mass. 1813) (No. 12,391).

10. *Chesterfield v. United States*, 159 F. Supp. 371, 375 (Ct. Cl. 1958).

11. *Pitcairn v. United States*, 547 F.2d 1106, 1126 (Ct. Cl. 1976).

12. *Embrex, Inc. v. Serv. Eng'g Corp.*, 216 F.3d 1343, 1353 (Fed. Cir. 2000).

13. *Madey v. Duke Univ.*, 307 F.3d 1351, 1362 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

14. *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 860 (Fed. Cir. 1984).

increased regulations concerned consumers due to the delayed entry of cheaper generics—delays exacerbated by patent extensions for delays in regulatory approval. In response, Congress developed an abbreviated approval pathway for generic drugs, including the statutory experimental use exception.¹⁵

The regulation of drugs has only become more stringent over time. It was only in 1962 that Congress amended the Food Drug and Cosmetics Act (FDCA) to require companies to submit proof of the drug's safety *and* efficacy for the marketed indication.¹⁶ Prior to that time, formulation safety was the primary concern.¹⁷

Today, the regulatory process for FDA approval of new drugs is relatively straightforward, but highly expensive and uncertain. After testing the new drug on animals,¹⁸ the company begins human testing in clinical trials to determine the safety and efficacy of the drug.¹⁹ The resulting data from the three-phased clinical trials is the basis for the evaluation of the drug.²⁰ Generally, if a drug's proposed benefits outweigh its known risks, the drug will be approved for sale.²¹

These increased safety and efficacy standards have increased the cost of drug development. The testing protocols and regulations required to comply with the FDCA cost millions of dollars.²² Since close to 90% of drugs in the clinical trial pipeline ultimately fail to

15. 35 U.S.C. § 101 (2012).

16. John P. Swann, *FDA's Origin and Functions: Part III*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm055118.htm> (last updated June 18, 2009).

17. For a general history of the development of the FDA, see John P. Swann, *FDA's Origin*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm124403.htm> (last updated June 23, 2014).

18. U.S. Food & Drug Administration, *How FDA Evaluates Regulated Products: Drugs*, U.S. DEP'T HEALTH & HUMAN SERV., <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm269834.htm> (last updated Apr. 4, 2012).

19. *Id.*

20. *Id.*

21. *Id.* The FDA, at this stage, has sixty days to decide to approve and file an application or not. U.S. FOOD & DRUG ADMIN., THE DRUG REVIEW PROCESS 1, *available at* <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/UCM195671.pdf>.

22. This number is highly disputed. Some studies range from approximately one hundred million to eight hundred million or more. MERRILL GOOZNER, \$800 MILLION PILL: THE TRUTH BEHIND THE COST OF NEW DRUGS 237, 239 (2004). But these studies often include capitalized costs of failed drug leads as well as opportunity costs. *Id.* at 10.

gain FDA approval,²³ pharmaceutical companies rely on patent protection to recoup the cost of development and generate a profit.²⁴

A patent can guarantee the pharmaceutical company a monopoly on sales of the drug for the life of the patent. As with the agricultural biotechnology industry, patents cover a large array of inventions within the drug development process. For instance, patents protect active ingredients of a drug, manufacturing practices, as well as specialized uses of the drug.

Due to increased regulation and the concomitant increased development cost, consumer prices of pharmaceuticals increased. Pharmaceutical companies command premium prices for patent-protected drugs due to the monopoly power granted by the drug's patent. Once the patent expires, other pharmaceutical companies may sell a drug previously covered by the patent. Once other companies enter the market selling the same drug, competition immediately drives down the price of the drug.²⁵

Unfortunately, generic drug companies initially had little incentive to invest in generic drug production. Before the Hatch–Waxman Act, generic drug companies were required to submit the same amount of safety and efficacy data as the branded drug company did in the initial filing, thus bearing both the cost of clinical trials as well as the low selling price of drugs once competition began.²⁶ Compounding the problem, patent protection prevented generic companies from beginning research on the generic form of a drug, resulting in a de facto patent extension.²⁷ These concerns over the availability of cheap generics for consumers after patent expiration led Congress to enact the Hatch–Waxman Act.²⁸

The Hatch–Waxman Act created an abbreviated approval pathway by which generic drug manufacturers could gain FDA approval. Under Hatch–Waxman, a generic company can file an Abbreviated New Drug Application (ANDA) and take advantage of the data submitted by the patented drug manufacturer by submitting

23. See Michael Hay et al., *Clinical Development Success Rates for Investigational Drugs*, 32 *NATURE BIOTECHNOLOGY* 40, 47 (2014).

24. Rebecca Eisenberg, *The Role of the FDA in Innovation Policy*, 13 *MICH. TELECOMM. & TECH. L. REV.* 345, 350 (2007).

25. See Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 *FOOD & DRUG L.J.* 187, 191 (1999).

26. *Id.* at 187.

27. See *id.*; Eisenberg, *supra* note 24, at 357.

28. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 35, and 42 U.S.C.).

only data to establish that the branded drug and the generic drug to be marketed are bioequivalent.²⁹ Obviously generation of this data requires use of the branded drug, an activity that would normally need permission from the patent owner if conducted during the patent term.

Therefore, in response to the limitation of the common law experimental use exception in *Roche*, the Hatch–Waxman Act amended the patent laws to establish a statutory experimental use exception to patent infringement for research on the drug during the patent period.³⁰ This statutory experimental use exception for generic drug companies resulted in quicker generic drug availability because research to establish bioequivalency is no longer an infringement of the patent protecting a branded drug. Consequently, consumers often are able to enjoy the benefit of generics on the day that the patent expires. This statutory experimental use exception has become a fundamental tenet of patent law for the pharmaceutical industry.

The statutory experimental use exception is found in 35 U.S.C. § 271(e)(1). Its language reads:

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

As applied to the pharmaceutical industry, the language of the statutory experimental use exception was read such that a “patented invention” is a patented drug—the “Federal Law which regulates the manufacture, use, or sale of drugs or veterinary biological products” is the provisions of the FDCA that cover the abbreviated approval process for generic drugs; and the use of the patented invention “solely for uses reasonably related to the development and submission of information” is the bioequivalency studies necessary

29. *Id.* § 101. Bioequivalency is defined as “the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study.” 21 CFR § 320.1(e) (2014).

30. 35 U.S.C. § 271(e)(1).

for generic approval.³¹ While these interpretations make sense in the context of the development of the Hatch–Waxman Act of which the statutory experimental use exception is a part, the language itself is actually quite broad. These ambiguities in the language of the statutory experimental use exception have led to a line of cases expanding the application beyond merely its use in the development of generic drugs. However, the statutory experimental use exception is not without its limitations.

B. Evolution of the Statutory Experimental Use Exception

The narrow conception of the statutory experimental use exception as applying solely to generic drug development prevailed until the Supreme Court heard the case of *Eli Lilly & Co. v. Medtronic, Inc.*³² At that time, the Supreme Court interpreted the application of the defense more broadly. Subsequent Supreme Court and Federal Circuit cases have further delineated the reach of the statutory experimental use exception as it applies to products other than generic drugs.

In *Eli Lilly*, the patent infringement allegations were based on the use of patented technology to develop a new medical device rather than a generic drug.³³ Like drugs, medical devices are also regulated under the FDCA,³⁴ though medical device regulations for pre-market approval are found in 21 U.S.C. § 360(e) rather than 21 U.S.C. § 355, which governs pre-market approval of drugs.

The *Eli Lilly* analysis of the extension of the statutory experimental use exception to medical devices relied on interpretation of various words and phrases within the statute. The Court first determined that the words “patented invention” within 35 U.S.C. § 271(e)(1) apply to all types of inventions rather than merely drug-related inventions.³⁵ Secondly, the *Eli Lilly* Court interpreted the phrase “a Federal Law which regulates the manufacture, use, or sale of drugs or veterinary biological products”³⁶ to include the entire statutory scheme of regulation by the FDCA.³⁷

31. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 675-76 (1990).

32. *Id.*

33. *Id.* at 661.

34. 21 U.S.C. §§ 301-395 (2012).

35. *Eli Lilly & Co.*, 496 U.S. at 665.

36. 35 U.S.C. § 271(e)(1).

37. *Eli Lilly & Co.*, 496 U.S. at 665-66.

While such a broad application of the statutory experimental use exception seems to open its application to any potentially patent-infringing activities used in conjunction with any sort of FDA-regulated product, the Court noted that potentially infringing uses are limited to those “reasonably related to the development and submission of information under” the FDCA in order to qualify for the defense.³⁸

Subsequently, a separate line of cases has dealt with the definition of “uses reasonably related to the development and submission of information” under the FDCA.³⁹ While the Supreme Court’s initial interpretation of the statute was quite broad, later cases from the Federal Circuit have defined limits on the use of the defense.

The leading Supreme Court case on the definition of uses that are “reasonably related” in the context of an FDA submission is *Merck v. Integra*.⁴⁰ In *Merck*, research was conducted on patented peptides without knowing which, if any, peptide eventually would lead to an FDA submission.⁴¹ The *Merck* Court held this research to be sheltered by the statutory experimental use exception. Thus, preclinical research on patented inventions is protected under the statutory experimental use exception as long as there is a reasonable basis to believe that the invention could become part of a submission to the FDA—even if it is actually never so included.

Again, the Supreme Court interpreted the application of the statute quite broadly. The Federal Circuit has followed that call for breadth in a number of ways. First, the Federal Circuit allowed the statutory experimental use exception to apply to the usage of the data resulting from the exempted infringement for non-FDA reporting purposes, *but* only so long as its initial research had originally been gathered via activities reasonably related to an FDA submission.⁴² More recently, the Federal Circuit approved of the application of the patent infringement defense in producing data for internal records

38. *Id.* at 674 n.6.

39. 35 U.S.C. § 271(e)(1).

40. 545 U.S. 193, 202 (2005).

41. *Id.* at 199.

42. *See, e.g.,* *Intermedics, Inc. v. Ventritex Co., Inc.*, No. 92-1076, 1993 WL 87405, at *5 (Fed. Cir. 1993); *Nexell Therapeutics Inc., v. AmCell Corp.*, 143 F. Supp. 2d 407, 421-22 (D. Del. 2001).

that were required to be “readily available for authorized inspection” by the FDA at any time—even if the records were never inspected.⁴³

The *Merck* Court did foresee some limitation on the types of studies covered by the statutory experimental use exception. For instance, the Court noted that basic research designed for information rather than the “intent to develop” a drug would not be covered by the defense.⁴⁴ Therefore, basic research institutions, such as universities and non-profits seeking to understand mechanisms of action rather than product development are unlikely to benefit from the statutory experimental use exception. Relying on *Merck*, the Federal Circuit held that the statutory experimental use exception does not apply to nonrequired, post-marketing infringing uses of a patented invention even if information is routinely reported to the FDA.⁴⁵

In addition to the line of cases regarding the term “reasonably related,” the Federal Circuit has also limited the application of the statutory experimental use exception in the context of infringing uses of research tools. In *Proveris Scientific Corp. v. Innovasystems, Inc.*, the Federal Circuit held that patented research tools that were not themselves subject to regulation by the FDA could not avail themselves of the statutory use exception.⁴⁶ For example, Innova’s device, used to measure the rate of a drug delivery product, was not FDA regulated, and thus the statutory experimental use exception did not apply—even though the drug delivery product was FDA regulated.⁴⁷ District courts have followed *Proveris* for molecular biology inventions used as research tools. For example, patented antisense nucleic acid molecules used to identify target molecules⁴⁸ and cloned receptors used to identify drug candidates⁴⁹ have been held to be research tools not eligible for shelter under the statutory experimental use exception.

As with the pharmaceutical industry, the agricultural biotechnology industry uses many of the same scientific techniques,

43. *Momenta Pharm., Inc. v. Amphastar Pharm., Inc.*, 686 F.3d 1348, 1357 (Fed. Cir. 2012).

44. *Merck*, 545 U.S. at 205-06.

45. *Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057, 1070 (Fed. Cir. 2011).

46. 536 F.3d 1256, 1265 (Fed. Cir. 2008).

47. *Id.*

48. *Isis Pharm., Inc. v. Santaris Pharma A/S Corp.*, No. 11CV02214 BTM (KSC), 2012 WL 4111157, at *1 (S.D. Cal. Sept. 19, 2012).

49. *PSN Ill., LLC v. Abbott Labs.*, No. 09C5879, 2011 WL 4442825, at *1 (N.D. Ill. Sept. 20, 2011).

faces similar challenges, and is subject to FDA regulation under the FDCA. The breadth of the application of the statutory experimental use exception along with its specific limitations will determine the value of patents in the agricultural biotechnology industry. But to understand the application and limitations of the statutory experimental use exception in agricultural biotechnology, it is first necessary to understand the industry, its patent strategy, and its regulation.

II. AGRICULTURAL BIOTECHNOLOGY INDUSTRY: REGULATION AND INTELLECTUAL PROPERTY PROTECTION

The agricultural biotechnology industry has experienced explosive growth over the past thirty years.⁵⁰ As described in Section III, intellectual property protection of living organisms and the insertion of foreign genes into plants both began in the early 1980s. Like the pharmaceutical industry, the agricultural biotechnology industry must comply with complicated regulations and relies on patent protection to recoup expense from GE crop development. The patent strategy of the agricultural biotechnology industry, like the pharmaceutical industry strategy, focuses on patenting several different aspects of GE crops and their production.

A. Developing and Regulating Genetically Engineered Crops

In the mid-nineteenth century, Gregor Mendel studied how traits, which are observable characteristics of an organism such as flower coloration, pass from one generation to the next in pea plants.⁵¹ His groundbreaking experiments began to reveal the rules of heredity.⁵² Almost one hundred years later, scientists would determine that DNA was the molecule that carried the information

50. For a full description of the history and regulation of the agricultural biotechnology industry, see Ritalin to RoundUp, *supra* note 7.

51. *Experiments in Plant Hybridization (1865)*, MENDELWEB, <http://www.mendelweb.org/Mendel.html> (last visited July 6, 2015). Gregor Johann Mendel (1822-1884) experimented on pea plant heredity between 1856 and 1863. Edward Edelson, *Gregor Mendel and the Roots of Genetics*, in OXFORD PORTRAITS IN SCIENCE 99, 99-100 (1999).

52. See Daniel L. Hartl & Vitezslav Orel, *What Did Gregor Mendel Think He Discovered?*, 131 GENETICS 245, 245 (1992).

resulting in these traits and that specific segments of DNA known as genes determine the observed traits of an organism.⁵³

By the 1970s, scientists had discovered the base knowledge and developed the first generation of tools needed for direct manipulation of DNA, a set of technologies known as recombinant DNA technology.⁵⁴ Recombinant DNA technology would quickly make its way into use in plants⁵⁵ and would eventually lead to the first commercial GE crop approved by the FDA—a GE tomato with a longer shelf life than conventionally developed tomatoes.⁵⁶ GE crops designed to be herbicide resistant or resistant to insect pests were developed shortly thereafter.⁵⁷ Today, nearly 90% of all soybeans and corn grown in the United States are genetically engineered.⁵⁸

Genetically engineered crops are regulated under a regulatory scheme known as the Coordinated Framework.⁵⁹ The Coordinated Framework rests on the underlying premise that GE crops developed through biotechnology are not fundamentally different from those crops developed using more conventional breeding techniques.⁶⁰ Therefore, existing regulations would be sufficient for regulation of GE crops. The Framework regulates these GE crops by relying on three main agencies: the FDA, the U.S. Department of Agriculture's

53. See, e.g., Oswald T. Avery, Colin M. MacLeod & Maclyn McCarty, *Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types: Induction of Transformation by a Desoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III*, 79 J. EXPERIMENTAL MED. 137, 156 (1944); see Maclyn McCarty, *Discovering Genes are Made of DNA*, 421 NATURE 406 (2003).

54. Ritalin to RoundUp, *supra* note 7, at 12 & n.40, 13 & n.41.

55. See e.g., Robert T. Fraley et. al., *Expression of Bacterial Genes in Plant Cells*, 80 PROC. NAT'L ACAD. SCI. U.S.A. 4803 (1983).

56. See *Agency Summary Memorandum Re: Consultation with Calgene, Inc., Concerning FLAVR SAVR™ Tomatoes*, FDA (May 17, 1994), <http://www.fda.gov/food/foodscienceresearch/biotechnology/submissions/ucm225043.htm#out20>.

57. See, e.g., *Recent Trends in GE Adoption*, USDA, <http://www.ers.usda.gov/data-products/adoption-of-genetically-engineered-crops-in-the-us/recent-trends-in-ge-adoption.aspx> (last updated July 14, 2014).

58. See *id.*

59. Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23302-93 (June 26, 1986). For a full description of the Coordinated Framework, see PEW INITIATIVE ON FOOD AND BIOTECHNOLOGY, *GUIDE TO U.S. REGULATION OF GENETICALLY MODIFIED FOOD AND AGRICULTURAL BIOTECHNOLOGY PRODUCTS* (2004), available at http://www.pewtrusts.org/~media/legacy/uploadedfiles/wwwpewtrustsorg/reports/food_and_biotechnology/hhsbiotech0901pdf.pdf [hereinafter PEW].

60. See PEW, *supra* note 59.

Animal and Plant Health Inspection Service (USDA-APHIS), and the Environmental Protection Agency (EPA).⁶¹ A single product is often regulated by more than one agency.

Acting under the authority of the FDCA, the FDA regulates the safety of agricultural biotechnology for consumption.⁶² In its 1992 Statement of Policy, the FDA clarified its interpretation of the application of the FDCA as it pertains to GE crops.⁶³ This policy basically provided that GE crops would be regulated as food additives under the Act.⁶⁴ However, GE crops are usually considered to be generally recognized as safe (GRAS) and, as such, much of the compliance with consultations and other FDA submissions are considered voluntary.⁶⁵ In spite of the technically voluntary nature of the regulations, developers of GE crops comply with the regulations to the extent that all GE crops that have gone through the mandatory USDA-APHIS review have also gone through the FDA voluntary process.⁶⁶

Like pharmaceuticals, these regulations are complicated, and the studies to create the GE crops and to develop the data for regulatory submissions require long-lines and millions of dollars. As a result, the agricultural biotechnology industry relies on patent protection to recoup costs in much the same way as the pharmaceutical industry.

B. Protecting Intellectual Property in Genetically Engineered Crops

Coinciding with the advancement of biotechnology, the industry building around GE crops was also assisted by changes in intellectual property law, allowing greater protection of crop plants. In 1930, the Plant Patent Act allowed for a type of patent protection of asexually reproduced plants.⁶⁷ However, most food-crop plants are sexually reproduced and thus not eligible subject matter for a plant patent of this type.⁶⁸ Over the next four decades, changes in the

61. *Id.*

62. 21 U.S.C. § 379dd (2012).

63. Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. 22984 (May 29, 1992).

64. *Id.*

65. PEW, *supra* note 59, at 20.

66. Nathanael Johnson, *The GM Safety Dance: What's Rule and What's Real*, GRIST (July 10, 2013), <http://grist.org/food/the-gm-safety-dance-whats-rule-and-whats-real/>.

67. 35 U.S.C. §§ 161-164 (2012).

68. §§ 161-164. Section 161 reads:

understanding of trait transmission in plants led Congress to pass the Plant Variety Protection Act of 1970 (PVPA),⁶⁹ which extended patent-like protection for sexually reproduced plants, including most crop plants.⁷⁰ However, the PVPA contained exemptions for research⁷¹ and for seed saving,⁷² making the intellectual property rights awarded by a PVPA certificate less valuable than rights that would be obtained if plants could be patentable subject matter for utility patents.

Originally, utility patents generally were not issued for living organisms.⁷³ However, along with the development and growth of biotechnology, the idea of utility patent protection for living organisms such as GE crops was also evolving during this time. The Supreme Court first examined the issue of utility patent protection for living things in 1980 with the case of *Diamond v. Chakrabarty*.⁷⁴

The Supreme Court in *Diamond v. Chakrabarty* determined that a live, but human-made, bacterium was patentable subject matter under 35 U.S.C. §101.⁷⁵ The *Chakrabarty* Court rejected the idea that man-made living things are products of nature and thus not patentable under 35 U.S.C. §101.⁷⁶ Five years later, the U.S. Patent

Whoever invents or discovers and asexually reproduces any distinct and new variety of plant, including cultivated sports, mutants, hybrids, and newly found seedlings, other than a tuber propagated plant or a plant found in an uncultivated state, may obtain a patent therefor, subject to the conditions and requirements of this title.

§ 161.

69. Plant Variety Protection Act, Pub. L. No. 91-577, 84 Stat. 1542 (1970) (codified as amended in scattered sections of 7 and 28 U.S.C.).

70. 7 U.S.C. §§ 2541, 2544 (2012).

71. § 2544 (“The use and reproduction of a protected variety for plant breeding or other bona fide research shall not constitute an infringement . . .”); see also Jim Chen, *The Parable of the Seeds: Interpreting the Plant Variety Protection Act in Furtherance of Innovation Policy*, 81 NOTRE DAME L. REV. 105, 133 (2005).

72. 7 U.S.C. § 2543 (2012) (“[I]t shall not infringe any right hereunder for a person to save seed produced by the person from seed obtained, or descended from seed obtained, by authority of the owner of the variety for seeding purposes and use such saved seed in the production of a crop for use on the farm of the person . . .”).

73. Ritalin to RoundUp, *supra* note 7, at 16; see also James Ming Chen, *An Agricultural Law Jeremiad: The Harvest Is Past, the Summer Is Ended, and Seed Is Not Saved*, 2014 WIS. L. REV. 235, 244 (discussing the reliance on trade secret protection by plant developers).

74. *Diamond v. Chakrabarty*, 447 U.S. 303, 305-06 (1980).

75. *Id.* at 309-10.

76. *Id.* at 310-11. “Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful

and Trademark Office (USPTO) adopted the Supreme Court's reasoning and expanded utility patent protection to transgenic plants as well as microorganisms.⁷⁷ In 2001, the Supreme Court affirmed the USPTO's granting of utility patent protection to GE plants.⁷⁸ During this time period, the agricultural biotechnology industry, then in its infancy, began to patent various aspects of the development of GE crops, including the genes coding for traits, methods for inserting genes, and the final genetically modified crops.⁷⁹

Utility patents can cover an extremely wide variety of inventions. 35 U.S.C. § 101 informs us that patentable subject matter includes any "new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."⁸⁰ This wide concept of patentable subject matter has allowed players within the agricultural biotechnology industry to gain valuable patents covering gene constructs, GE plants, and research tools.

An example of a utility patent from the agricultural biotechnology field can be found in U.S. Patent No. 6,537,756 ('756), a patent directed at the invention of an insecticidal protein called CryET29 produced by a gene isolated from the *Bacillus thuringiensis* bacteria.⁸¹ Claim 1 of the '756 patent covers the isolated DNA sequence of the CryET29 gene as well as minor alterations of that gene, which would still produce an insecticidal protein.⁸² The '756 patent also claims shorter portions of the gene

improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101 (2012).

77. See *Ex parte Hibberd*, 1985 WL 71986 (B.P.A.I. Sept. 24, 1985) (ruling that plants could be proper subject matter for a patent under 35 U.S.C. § 101 even though the same may be protected under the Plant Patent Act or the Plant Variety Protection Act).

78. *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 127 (2001).

79. John H. Barton, *Acquiring Protection for Improved Germplasm and Inbred Lines*, in *INTELLECTUAL PROPERTY RIGHTS IN AGRICULTURAL BIOTECHNOLOGY* 23, 24 (F.H. Erbisch & K.M. Maredia eds., 2004).

80. § 101.

81. U.S. Patent No. 6,537,756 (filed Jul. 6, 2000).

82. *Id.* at col. 54 ll. 52-57 ("A purified nucleic acid segment consisting of the nucleic acid complement of SEQ ID NO:1 or a sequence encoding an insecticidally active protein which hybridizes to the sequence of SEQ ID NO:1 under stringent hybridization conditions comprising about 0.02M to about 0.15M NaCl and temperatures of about 50° C. to about 70° C.").

sequence⁸³ and the use of the claimed gene within another nucleic acid construct.⁸⁴ Also claimed is the ability to insert the CryET29 gene into another organism.⁸⁵ Further claims specifically identify these organisms as including other types of bacteria⁸⁶ or a plant⁸⁷ such as corn, wheat, or a fruit tree.⁸⁸ By gaining a patent with these claims, the patent owner has obtained intellectual property rights allowing the owner to exclude others from (1) isolating the CryET29 gene or a relatively short portion of that gene; (2) using the CryET29 gene in a nucleic acid construct such as a plasmid; and (3) using the CryET29 gene to create almost any type of GE organism.⁸⁹

However, the recent Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics Inc.*⁹⁰ has narrowed the ability of inventors to claim some gene sequences by limiting the definition of patentable subject matter in living organisms.⁹¹ Specifically, *Myriad* addressed whether isolated DNA sequences of naturally occurring genes were patentable subject matter.⁹² The Court held that merely isolating genes, i.e., removing a DNA sequence from its normal environment of the organism's genome, does not make them patentable subject matter.⁹³ An isolated DNA sequence that matches a sequence found in an organism is not patentable subject matter as it is found in nature.⁹⁴ The *Myriad* holding may have significant impact on patent protection of the genes underlying the valuable traits used in GE crops.

83. See *id.* at col. 54 ll. 62-64 (“An isolated nucleic acid segment consisting of at least a forty-five basepair contiguous nucleic acid sequence from SEQ ID NO:1.”).

84. See *id.* at col. 55 ll. 1-7. “The nucleic acid segment of claim 2, further comprising a recombinant vector.” ’756 Patent at col. 55 ll. 1-2.

85. See *id.* at col. 55 ll. 8-9 (“A recombinant host cell comprising the nucleic acid segment of claim 2.”).

86. See *id.* at col. 55 ll. 14-16 (“The recombinant host cell of claim 12, wherein said bacterial cell is an *E. coli*, *B. thuringiensis*, *B. subtilis*, *B. megaterium*, or a *Pseudomonas* spp. cell.”).

87. See *id.* at col. 55 ll. 21-22 (“The recombinant host cell of claim 15, further defined as a plant cell.”).

88. *Id.* at col. 55 ll. 23-25 (“The recombinant host cell of claim 16, wherein said plant cell is a corn, wheat, turf grass, potato, vegetable, ornamental, or fruit tree cell.”).

89. *Id.* at col. 4 ll. 1-11.

90. *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013).

91. *Id.* at 2111, 2120.

92. *Id.* at 2111.

93. *Id.* at 2117-18.

94. *Id.* at 2111.

Under *Myriad*, naturally occurring gene sequences such as the CryET29 gene claimed in the '756 patent are no longer patentable subject matter even when isolated from the original genome. However, the *Myriad* court also held that cDNA, a relatively minor laboratory alteration of a gene's sequence, was patentable subject matter because that altered sequence differs from the sequence found in nature.⁹⁵ The *Myriad* holding suggests that relatively minor alterations to otherwise naturally occurring genes may allow those genes to be patentable subject matter.⁹⁶ Future court decisions may well use this reasoning to hold that alterations to a naturally occurring gene, such as adding promoter and enhancer sequences,⁹⁷ placement into a specific vector, or the removal of portions of the gene sequence, render the altered DNA sequence patentable subject matter. Therefore, in the '756 patent, the claims directed specifically at the isolated CryET29 gene would be unlikely to be upheld under *Myriad*, but the use of the CryET29 gene in other nucleic acid constructs and the use of the gene in creating GE crops are likely to remain patentable subject matter.

Also commonly observed in the agricultural biotechnology field are patents directed at research tools. Research tools are inventions with which companies conduct research rather than inventions on which research is conducted.

One of the most widely used research tools over the last few decades is the method of inserting foreign DNA into plant cells (a process known as transformation) using *Agrobacterium*. There are numerous patents associated with this basic technology and improvements on it. One such patent is U.S. Patent No. 6,603,061 ('061), which is directed towards an improvement on *Agrobacterium*-mediated transformation of plant cells in which an antibiotic is used on the cells to prevent too many copies of the foreign DNA from being inserted.⁹⁸ Claim 4 specifically covers an

95. *Id.* at 2119.

96. *Id.* at 2112, 2119. While the *Myriad* Court declared cDNA to be patentable subject matter, the other requirements for obtaining a patent—novelty, non-obviousness, and utility—still apply. Given the routine nature of cDNA conversion in modern laboratories, the non-obviousness of recent cDNA patents may be in question.

97. Promoter and enhancer regions are involved with controlling transcription of a gene, which is the first step performed in the cell toward producing a protein such as the CryET29 protein.

98. U.S. Patent No. 6,603,061 col. 40 ll. 31-52. Claim 4 of '061 reads:
A method of transforming a plant cell or plant tissue using an *Agrobacterium* mediated process comprising the steps of:

Agrobacterium-mediated transformation of a dicotyledonous variety of plant in which an antibiotic is used, followed by culturing the transformed cells and growing plants from them. Research tool inventions are important because they are the tools by which products are created.

III. LIMITATIONS TO THE APPLICATION OF THE STATUTORY EXPERIMENTAL USE EXCEPTION IN THE AGRICULTURAL BIOTECHNOLOGY INDUSTRY

Although I argue that the statutory experimental use exception should apply to the agricultural biotechnology industry in a separate Article,⁹⁹ it is important to recognize that, as in the pharmaceutical industry, there are limitations as to what will be covered by the defense to patent infringement. Specifically, research conducted for non-FDA activities and using patented research tools may not be eligible for the defense. These limitations to the statutory experimental use exception will allow the patents to retain real value for the companies who invested in the creation of the patented inventions.

A. Research Conducted for Submission to Other Agencies

Like pharmaceuticals, GE crops are regulated by the FDA—and it is this regulation that is the basis for my arguments as to why the statutory experimental use exception should apply to the

inoculating a transformable plant cell or tissue from a dicotyledonous plant with *Agrobacterium* containing at least one genetic component capable of being transferred to the plant cell or tissue in an inoculation media containing an effective amount of at least one antibiotic that inhibits or suppresses the growth of *Agrobacterium*;

co-culturing the transformable plant cell or tissue after the inoculating step in a medium capable of supporting growth of plant cells or tissue expressing the genetic component, said medium not containing said antibiotic;

selecting transformed plant cells or tissue; and

regenerating a transformed plant expressing the genetic component from the selected transformed plant cells or tissue.

Id.

99. Ritalin to RoundUp, *supra* note 7.

agricultural biotechnology industry. However, unlike pharmaceuticals, GE crops are regulated under a Coordinated Framework that involves the FDA, USDA, and EPA working together to regulate different aspects of the crop for production.¹⁰⁰

Due to this tri-agency regulatory scheme, the developer of a new GE crop will conduct potentially infringing uses to develop submissions for the USDA or the EPA in addition to the FDA. The statutes underlying the USDA and EPA portions of the Coordinated Framework generally have no such statutory experimental use exception for patent infringement.¹⁰¹

Thus, while the *Telectronics* Court clarified that the statute allows data produced under the statutory experimental use exception to be also used for non-FDA reporting purposes,¹⁰² experiments designed solely to comply with mandatory USDA or EPA regulations would infringe any applicable patents. It would likely be extremely difficult for a GE crop developer to design all experiments such that all infringing activities are directed in some manner toward FDA regulations since the USDA and EPA have widely varying requirements directed at issues other than food safety. Additionally, to avoid infringement liability, companies would be required to prove that each and every experiment or field trial was conducted to gather data to be submitted to the FDA. Keeping track of these resultant agency submittals would be a logistical nightmare. If an experiment failed to be conducted to create data for submission to the FDA, then the company would be liable for patent infringement. The potential for confusion would increase the cost of research oversight and the risk of patent infringement liability.

B. Research Conducted Using Patented Research Tools

Another limitation to the statutory experimental use exception that would be important for the value of patents in the agricultural biotechnology industry is the research tool limitation. As in the pharmaceutical industry, protecting research tools incentivizes companies to invest in developing tools for creating new GE crops.

100. For a full description of the Coordinated Framework, see PEW, *supra* note 59.

101. Though some of the EPA regulatory power is based in the FDCA. See Carter-Johnson, *supra* note 7, for comments pertaining to expansion of the statutory use exception beyond FDA regulations.

102. *Telectronics Pacing Sys., Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1524 (1992).

The *Proveris* holding restricting the application of the statutory experimental use exception from research tools will yield a broad base of protection for the industry.¹⁰³

Research tools, such as the methods to create GE crops covered by the '061 patent, are not regulated by the FDA.¹⁰⁴ Patent protection for methods of creation allows companies monopolies far upstream in the research spectrum. Because the statutory experimental use exception would not be available as a defense for infringement of the patents protecting these research tools, competitors would be forced to license the patented research tools or invent new methods to insert the gene of interest into the crop to be produced. Thus, the value of these patents would be retained even if the statutory experimental use exception applied to the industry.

Additionally, many of the same types of molecular biology research tools used by the pharmaceutical industry, such as antisense nucleic acids and receptors, will be important in research underlying the determination of which genetic modifications will be most important in a given crop. Because courts have previously held that the statutory research exception does not apply to these types of research tools,¹⁰⁵ competitors will again need to license the patents to use these tools to develop new products. Furthermore, it is likely nucleic acid constructs such as those claimed in the '756 patent would be considered research tools if the plasmid is not found in the final regulated genetically modified crop but rather is used in its production. In each case, the research tool patent would retain much of the valuation it had before the implementation of the statutory experimental use exception in the agricultural biotechnology industry.

CONCLUSION

As the patents surrounding the initial agricultural biotechnology crops are expiring, interest will turn to generic versions of crops, much like drugs. The Hatch–Waxman Act is one model for development of a generic industry. Therefore, as we think about whether Hatch–Waxman-izing the agricultural biotechnology

103. *Proveris Scientific Corp. v. Innovasystems, Inc.*, 536 F.3d 1256, 1265 (2008).

104. *See, e.g., id.*

105. *See Isis Pharm., Inc. v. Santaris Pharma A/S Corp.*, No. 11CV02214 BTM (KSC), 2012 WL 4111157 (S.D. Cal. 2012); *PSN III, LLC v. Abbott Labs.*, No. 09 C 5879, 2011 WL 4442825 (N.D. Ill. 2011).

industry is appropriate, consideration should be given to what impact the application of the statutory experimental use exception would have on the industry. This Article on the limitations of the statutory experimental use exception complements my longer discussion as to why the defense should apply in the agricultural biotechnology industry. In short, patents in the industry would still retain much value in the event the statutory experimental use exception is applied.