PHARMACEUTICAL INVENTIONS: A PROPOSAL FOR RISK-SENSITIVE REWARDS

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I. INTRODUCTION

Patent grants are insensitive to economic considerations such as investment risks and expectations. In the pharmaceutical industry, the granting of identical rewards for different undertakings results in the diversion of valuable resources to low risk, high return industrial segments rather than to innovative new research.[1] The rewards being referred to in this article are the monopoly rights embodied by the term and scope of patent claims and their extensions.[2]

Patent rewards are economic incentives to innovate.[3] Without rewards, there is little motivation to invest into new and less predictable research and development. Indiscriminate rewards tend to result in the onslaught of sophisticated imitation rather than innovation.[4] Companies are constantly coming up

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* Meso Scale Diagnostics, LLC. Opinions expressed herein are solely the author's and not of the company. Special thanks to Mark R. Patterson, Esq., Peter T. Lansbury, Jr., Ph.D. and to my wife Ingrid Hsu for her patience and help in preparation of this manuscript.

1 Peter T. Lansbury, Jr., *An Innovative Drug Industry? Well, No*, Wash. Post B2 (Nov. 16, 2003) ("[T]he system that currently regulates the development and approval of new drugs discourages innovation.").

2 35 U.S.C. §154(a)(1) (2000) (providing the "right to exclude others from making, using, offering for sale, or selling the invention").

3 *Mazer v. Stein*, 347 U.S. 201, 219 (1954) ("[T]he economic philosophy behind the clause empowering Congress to grant patents and copyrights is the conviction that encouragement of individual effort by personal gain is the best way to advance public welfare through the talents of authors and inventors in 'Science and useful Art.'").

4 *See* Christopher Rowland, *Drug Makers Court Small Firms in Push to Fill Thinning Pipelines*, Boston Globe D1 (Mar. 29, 2005) ("[T]here has been a steady decline in the number of genuinely new drugs . . . ."); *see also* Public Citizen Congress Watch, *Rx R&D Myths: The Case Against the Drug Industry's R & D "Scare Card"*, 13, tbl. 5 (July 2001) [hereinafter *Rx R&D Myths*] ("[T]he FDA classified 53% of the drugs approved between 1982 and 1991 as offering 'little or no therapeutic gain.'"); The Natl. Inst. for Health Care Mgt. Research & Educ. Found., *Changing Patterns of Pharmaceutical Innovation* 3-9 (May 28, 2002) (FDA

with drugs which have only marginal new benefits for conditions[5] for which treatments are already available (usually called copycat or me-too drugs).[6] At the same time, potential drugs for diseases that have high investment risks or low expected return on investment[7] attract little interest from the pharmaceutical industry; these are often a result of diseases that have complex biology or affect relatively small portions of the population.[8] Sometimes firms remove promising drugs from studies because the expected returns cannot support the expense of further clinical trials.[9]

This article proposes the use of patent incentives to promote the redistribution of available monetary and human resources towards areas of public need, such as drug development for currently incurable diseases and conditions.

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noting that only 15% of the 1035 drugs approved between 1989 and 2000 provided any significant improvement over existing medicines).

5 The terms disease, condition, disorder are used indiscriminately throughout the article.

6 Philip Ma & Rodney Zemmel, *Value of Novelty?*, 1 Nat. Revs.: Drug Discovery 571, 571-72 (2002) (of thirty-one "blockbuster" drugs (those with annual sales of $1 billion or more) launched between 1992 and 2001, twenty-three were me-too drugs for common conditions such as allergies and inflammation). Contrast copycat drugs to novel drug that use treatable diseases as test models for new technologies. *See* Zachary Zimmerman, *Silence is Golden*, Bio-IT World 12 (Dec. 2004) (describing recently filed INDAs for the treatment of age-related macular degeneration from Acuity Pharmaceuticals and Sirna Therapeutics and imminent filings from Alnylam Pharmaceuticals. The treatments for this condition already exist or are in trials (from Eyetech and Genentech), but the new drugs make the first use of RNA interference technology.). Also contrast to generic drugs that are exact copies of the patented medicines and are not entitled to patent protection.

7 The risk of failure is one recognized aspect of the total risks associated with drug discovery. The article however does not address additional risks. *See* Joseph A. DiMasi, *Risks in New Drug Development: Approval Success Rates for Investigational Drugs*, 69(5) Clinical Pharmacology & Therapeutics 297 (May 2001) [hereinafter *Risks in New Drug Development*]. One example of additional risks is Thalidomide marketed to cancer patients at almost five-fold greater price than to AIDS patients due to the strong political activism of AIDS groups. *See* Geeta Anand, *How Drug's Rebirth as Treatment for Cancers Fueled Price Rises*, Wall St. J. A1, A18 (Nov. 15, 2004).

8 J.R. Minkel, *Academia Thrives on CNS Neglect*, Drug Discovery & Dev. 24 (Oct. 1, 2004) (citing Lansbury, "[t]he only hope for these diseases is to have a group like ours get lucky. . . . It's desperation."); *see also* Lansbury, *supra* n. 1, at S54 (citing Beth Borowsky, senior principle scientist at Aventis Pharmaceuticals, "[t]he low-hanging fruit in CNS drug discovery [is] gone.").

9 Amy D. Marcus, *A Patient's Quest to Save New Drug Hits Market Reality*, Wall St. J. A1, A17 (Nov. 16, 2004).

This redistribution is ideally achieved without an increase in the overall costs to consumers.[10]

Making patent rewards proportional to research and development risks and inversely proportional to expected investment returns may guide pharmaceutical firms to invest into socially desirable projects.

II. BACKGROUND

A. Patent and Regulatory Laws do not Account for Economic Considerations

Formally articulated for the first time by Judge Pauline Newman, "[t]he encouragement of investment-based risk is the fundamental purpose of the patent grant . . . ."[11] The statement was based on principles that were historically

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[10] The goals of maintaining accessible prices and providing treatments are interrelated. First, the high costs of drugs paid by patients deplete available funds and consequently affect the redistribution. Second, price may become prohibitive and the drug, although actually available to patients, will in fact be inaccessible. *See* Amy D. Marcus, *Price Becomes Factor in Cancer Treatment*, Wall St. J. D1, D5 (Sept. 7, 2004). Further, the analysis of pharmaceutical research and development in Europe justifies increased costs. Citing Bain & Company's study, "Addressing the Innovation Divide":

> Europeans spent approximately 60% less than Americans on pharmaceuticals in 1992 and the gap has doubled since then, while European governments spent approximately 30% less per capita than the US. [P]harmaceutical innovation has basically 'followed the money' . . . . Today the Europe's share [of the pharmaceutical market] is down to 18%, while that of the U.S. has jumped to 62%. . . . Bain's research shows that the social and economic costs to Europe, in the form of delayed access to drugs, poorer health outcomes, decreased investment in research capabilities, and a drain placed on high-value pharmaceutical jobs, undermine the 'free ride' approach.

See Kimberly S. Cleaves, *Imbalanced Innovation: European "Free Ride" in R&D Has Its Limits*, Modern Drug Discovery, 23-24, 23 (July 2004) [hereinafter *Imbalanced Innovation*]. In Europe, price regulation significantly retards both the development of new drugs and the public access to new treatments. *Id.*

[11] *Patlex Corp. v. Mossinghoff*, 758 F.2d 594, 599 (Fed. Cir. 1985), *modified*, 771 F.2d 480 (Fed. Cir. 1985).

important in deciding intellectual property disputes.[12] The term and scope of patent rewards, however, do not account for economic factors.[13]

A basic patent term is always fixed at 20 years from the earliest priority date.[14] The scope of claims is determined in accordance with the scope of the enabling disclosure regardless of economic considerations.[15] The limiting of a patent term allows others to practice the invention after the patent expires. This limits deadweight losses associated with monopolies, but also inadvertently encourages the tying of resources in anticipation of jumping on the bandwagon.[16] The outdated "stuck in the 60's" standards of patentability also promote low risk sophisticated imitations rather than innovation.[17]

A recent Federal Trade Commission (FTC) report also reflects the need to view patent protection as an integral part of the economic system.[18] The report discusses the differences between "head start innovation," "follow-on innovation," and "follow-on innovation in the face of a blocking patent or multiple existing patents."[19] The FTC proposed that the US Patent and Trademark Office

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12 *See e.g. Zacchini v. Scripps-Howard Broadcasting Co.*, 433 U.S. 562, 573 (1977) (encouraging investment of stunt performer's time and effort); *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480 (1974) (patent law promotes the progress of "useful arts" by encouraging inventors "to risk the often enormous costs in terms of time, research, and development.").

13 *See* 35 U.S.C. §§101-03, 112; *see also* Donald S. Chisum et al., *Principles of Patent Law* 323, 514, 707 (2d ed., Found. Press 2001).

14 *See* 35 U.S.C. §154(a) (codifying US obligations under Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994); Marrakesh Agreement Establishing The World Trade Organization, *Annex IV, Legal Instruments—Results of the Uruguay Round*, 33 I.L.M. 81 (1994).

15 35 U.S.C. §112; *see also* Chisum et al., *supra* n.13, at 707.

16 *See* Cleaves, *supra* n. 10, at 23; *see also generally supra* n. 6.

17 Lansbury, *supra* n. 1, at S51, S54 ("[Non-obviousness] requirement is currently interpreted as though that person's 'schooling' ended in 1960. Specifically, the obviousness of the discovery depends solely on chemical structure. . . . Now, though, drug discovery is largely target driven, and it is no surprise that two [compounds] . . . with very different structure have the same *in vivo* effect. Yet the patent law still allows both compounds to be patented. This archaic interpretation of the criterion of obviousness is the origin of the copycat school of drug development."). *See also* Mark L. Hayman, *Unpredictable Inventions: Patenting Bionanotechnology Inventions Presents Certain Enabling Challenges*, Modern Drug Discovery 19-20 (Nov. 2004).

18 FTC Report on Antitrust and Intellectual Property, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy* (2003) (available at http://www.ftc.gov/os/2003/10/innovationrpt.pdf) [hereinafter *FTC Report*].

19 *See* James B. Kobak, *The Government's IP/Antitrust Hearings: Where are We and Where do We Go From Here?*, Practising Law Institute, Intell. Prop. Antitrust 2004, 383, 388 (PLI 2004).

(USPTO) should consider potential harm to competition by adding a policy-based component to the otherwise technical review of patent applications.[20] The practicality of this proposal as well as the role of the USPTO in place of congress or the courts is controversial.[21]

1. Pharmaceutical Industry is Sensitive to Economic Stimulus

Anthony T. Kronman suggested that the law should promote the deliberate acquisition of information.[22] Similarly, patent law should encourage monetary investment into the research and development of the treatments for currently incurable diseases and conditions, because monetary investment often correlates with the successful development of the final product.[23] It is the essence of patent policy to encourage innovation through *ex post facto* rewards.[24]

2. Patent and Regulatory Law Has Three Mechanisms to Fine Tune Rewards

The industry is sensitive to positive and negative economic incentives such as: (1) adjustments to the lengths of a legally granted monopoly; (2) the interpretation of the scope of monopoly; and (3) the fear of compulsory licensing.

a. Adjustments to the Lengths of a Legally Granted Monopoly

The industry is specifically sensitive to the period of the monopoly granted by the patent term and its extensions. For example, the Best Pharma-

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20 *Id.* at 396-98, 400, 403-04.

21 *Id.* at 400, 404; *see also* Hillary Green, *Competition Perspective on Patent Law Substance and Procedure; An Overview of the FTC/DOJ Hearing and the FTC Report*, 18-SPG Antitrust 34, 36 (2004).

22 Anthony T. Kronman, *Mistake, Disclosure, Information, and the Law of Contracts*, 7 J. Legal Stud. 1 (1978) (noting that Kronman's theory has garnered some criticism); *See* Andrew Kull, *Unilateral Mistake: The Baseball Card Case*, 70 Wash. U. L.Q. 57 (1992).

23 *See* Cleaves, *supra* n. 10, at 23 (explaining the success of the pharmaceutical industry in the U.S. because "pharmaceutical innovation has basically 'followed the money'").

24 Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. Chi. L. Rev. 1017, 1024 (1989); *see also* John F. Duffy, *Rethinking The Prospect Theory of Patents*, 71 U. Chi. L. Rev. 439 (2004).

ceuticals for Children Act of 2002[25] provides incentives to conduct pediatric drug testing by granting six months pediatric market exclusivity.[26] The Act successfully stimulated investment into pediatric drug testing,[27] but was insufficient to attract pediatric testing for drugs that only have a relatively small target market.[28] Further, Congress had previously enacted The Pediatric Research Equity Act of 2003, which acted to penalize firms for marketing drugs without pediatric testing.[29]

The Hatch-Waxman Act provides additional market exclusivity for new drugs to compensate for the delays in the FDA approval process.[30] Extensions are often warranted when the FDA approval process stretches for more than a decade, leaving inventors with a short patent term, or no term at all.[31]

The Orphan Drug Act rewards developers of orphan drugs (drugs for diseases affecting less than 200,000 patients or drugs for diseases affecting more than 200,000, when there is no reasonable expectation to recover research and development costs)[32] with seven years of market exclusivity plus certain tax

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25 *The Best Pharmaceuticals for Children Act of 2002*, Pub. L. No. 107-109, 115 Stat. 1408 (2002) (formerly the *FDA Modernization Act of 1997*, Pub. L. No. 105-115, 111 Stat. 2296 (1997)); *see also* Michael S. Labson, *Pediatric Priorities: Legislative and Regulatory Initiatives to Expand Research on the Use of Medicines in Pediatric Patients*, 6 J. Health Care L. & Policy 34 (2002).

26 Phillip B. C. Jones, *Pediatric Drug Testing: Not Child's Play*, Modern Drug Discovery 21-22 (Mar. 2004) (describing post-patent or non-patent (e.g., in case of antibiotics) extensions) [hereinafter *Pediatric Drug Testing*].

27 *Id.* at 21-22 ("[T]he offer of additional market exclusivity has been a success . . . . [T]he FDA had issued 284 requests for pediatric studies; 228 were based on proposals from industry.").

28 *Id.* at 22.

29 *Pediatric Research Equity Act of 2003*, Pub. L. No. 108-155, 117 Stat. 1936 (2003) (codified as 21 U.S.C. §335(c)). Under the Act, the FDA can issue a request for pediatric testing. Jones, *supra* n. 26, at 22 ("If a company fails to submit an assessment on a drug or biologic, the product may be considered misbranded and subject to enforcement action, including injunction, prosecution, or seizure.").

30 *The Drug Price Competition and Patent Term Restoration Act of 1984*, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. and 35 U.S.C.); *see* Rebecca S. Eisenberg, *Lecture: Patents, Product Exclusivity, And Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 Fordham L. Rev. 477, 481-84 (2003).

31 *See* Andrew Pollack, *Defensive Drug Industry: Fueling Clash Over Patents*, N.Y. Times A6 (Apr. 20, 2001); *see also* Barbara M. Bolten & Tracy DeGregorio, *Trends in Development Cycles*, 1 Nat. Revs.: Drug Discovery 335, 335 (2002) ("requir[ing] approximately 12-15 years to bring a new compound to the market").

32 *See* Sheila R. Shulman and Michael Manocchia, *The US Orphan Drug Programme: 1983-1995*, 12(3) Pharmacoeconomics 312, 314 (Sept. 1997).

credits.[33] In the 20 years since the Act was passed, over 200 orphan drugs have been introduced into the market and an additional 900 are in various stages of development.[34] This represents a large increase over the fewer than ten orphan drugs introduced during the decade preceding passage of the Act, indicating that the pharmaceutical industry can be persuaded through such means to develop treatments that are not immediately profitable.[35] The Orphan Drug Act by itself, however, is insufficient to spur investment into drug development for complex diseases affecting smaller patient populations.[36]

Although the economics of the optimal patent term are very complex,[37] an extension to the basic term may be sufficient to provide the additional stimulus needed to redirect investments to the under-researched areas.

b. Interpretation of the Scope of Monopoly

The scope of allowed claims is another variable which may affect drug development. There is no general agreement on the optimal scope of patent claims, but there are two dominant theories.[38]

Kitch's "prospect theory" suggests that patent rights are analogous to mining rights or "prospect rights" as they developed in the American West.[39] When a miner first struck gold, he could claim prospecting rights which allowed him to exclude others from mining in the area.[40] He could also mine as he wished.[41] The grant of broad patent rights also goes beyond merely rewarding for the invention already made; it allows the inventor the prospective control of

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33 *Orphan Drug Act*, Pub. L. No. 94-414, § 526(a)(2), 96 Stat. 2049 (1982) (codified as amended at 21 U.S.C. § 360bb (2000)).

34 National Organization for Rare Disorders, *Celebrating 20 Years of Service* (2003) (available at http://www.rarediseases.org/briefs/nord_20th_article).

35 *Id.*

36 *See supra* n. 8 and accompanying text.

37 *See* W. Nordhaus, *Invention, Growth, and Economic Welfare: A Theoretical Treatment of Technological Change and Economic Welfare*; F.M. Scherer, *Nordhaus' Theory of Optimal Patent Life: A Geometric Reinterpretation*, 62 Am. Econ. Rev. 422-27 (1972).

38 *See* Duffy, *supra* n. 24, at 439.

39 Edmund W. Kitch, *The Nature and Function of the Patent System*, 20(2) J.L. & Econ. 265, 266-67 (Oct. 1977).

40 *Id.*

41 *Id.*

the development of his invention.[42] The theory is grounded in the assumption that the inventor is interested in bringing the invention to market and enlarging its patent value.[43] While this model works well in situations where small entities rely on a single invention in their portfolio, the theory does not explain patent blocking[44] or technology suppression.[45]

The theory proposed by Merges and Nelson suggests that the law should favor granting patents with narrow scopes in order to stimulate competition for improvements, rather than the favoring dominance of a pioneer firm.[46] The theory attempts to balance incentives to the inventor with the risk of under use of the invention due to patent monopoly.[47] Excessive breadth of patent claims would tend to discourage research into improvements, because "proprietary control of technology tend[s] to cause 'dead weight' costs due to the restrictions on use."[48] For Merges and Nelson, the optimum scope of patent claims is a scope that still promotes competition in research.[49]

A judicial review component is crucial to affirming the appropriate scope of claims because the courts often have the benefits of hindsight during litigation, unlike the USPTO's view at the initial granting of the patent. The courts can declare the scope of claims excessive and scale back the breadth of "land-grabbing" claims.[50]

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42 *Id.* at 267 ("an incentive to make investments to maximize the value of the patent without fear that the fruits of the investment will produce unpatentable information appropriable by competitors").

43 *Id.*

44 *See* Leila Abboud, *How Drug Giant Keeps Monopoly On 60-Year-Old Pill*, Wall St. J. A1, A8 (Sep. 9, 2004) (describing a fifteen year long attempt by Barr Laboratories to bring a copy of the off-patent Premarin to the market and the manipulations by Wyeth to block the entry); *see also* Rick Murdock & David Fisher, *Patient Number One*: *A True Story of How One CEO Took on Cancer and Big Business in the Fight of His Life* 254 (Crown Publishers 2000) (explaining that CellPro was driven out of business by Baxter where Baxter used a patent licensed from Johns Hopkins University when it did not have an alternative product).

45 *See* Charles A. Black, *The Cure for Deadly Patent Practices: Preventing Technology Suppression and Patent Shelving in the Life Sciences*, 14 Alb. L.J. Sci. & Tech. 397 (2004).

46 Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 Colum. L. Rev. 839, 843 (1990).

47 *Id*. at 868.

48 *Id*. at 870-71.

49 *Id*. at 872.

50 *In re Wallach*, 378 F.3d 1330, 1335-36 (Fed. Cir. 2004). As one source comments:

> Claims to DNA molecules encoding an isolated protein, where only a part of the amino acid sequence is known at the time of filing of the patent application, do not satisfy the written description requirement for nucleotide claims,

c. Imposing Compulsory Licensing

Finally, an important but dormant mechanism for discouraging patent abuse is compulsory licensing, a situation in which a court or regulatory agency orders a patent holder to grant other parties a license to use his invention. There is no U.S. law that requires compulsory licensing of patent rights,[51] except in two limited circumstances. The first exception is the "march in" provision of the Bayh-Dole Act,[52] which allows courts to mandate compulsory licensing of inventions developed with public funds. This provision has never been applied, and it is unclear when or if "march in" compulsory licensing can ever be justified.[53] The second exception is the narrowly tailored "Bolar exception" of the

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even when the function and molecular weight of the intact protein are also described.

William L. Warren & Devesh Srivastava, *Description Requirements for Patenting Genes: Encoding Partially Characterized Proteins*, 24 Genetic Engr. News 10 (Nov. 1, 2004); *see U. of Rochester v. G.D. Searle Co.*, 358 F.3d 916 (Fed. Cir. 2004) (invalidating the claim when the University of Rochester attempted to "reach through" and claim chemical compounds discoverable by the invented methods when no discovery of compounds occurred at the University); *see* Merges & Nelson, *supra* n. 46, at 843; *see also generally* Miranda M. Biven & Matthew R. Cohen, *Reach-Through Royalties in Research Tool Licenses: Bayer AG v. Housey Pharmaceuticals*, Kirkland & Ellis Biotech Update 1 (Winter 2002); *see also* Phillip B. C. Jones, *When the 'Reach-Through' Exceeds the Grasp*, Modern Drug Discovery 21 (July 2004) (reviewing reach-through); *but cf. Bayer AG v. Housey Pharms., Inc.*, 169 F. Supp. 2d 328, (D. Del. 2001) (affirming the legality of "reach-through" licensing).

51 *See* H.R. 3235, 107th Cong. § 158(a) (Nov. 6, 2001) (compulsory licensing failing to garner support in Congress); Black, *supra* n. 45, at 405.

52 35 U.S.C. §203(a).

53 *See* Murdock & Fisher, *supra* n. 44, at 254-57 (explaining that the most notorious march-in case is the petition of CellPro, which was advocated by Senator Bayh himself. CellPro was driven out of business by Baxter using a patent licensed from Johns Hopkins University. At the time Baxter did not have an alternative product. The petition was thwarted by Baxter's assurances that the treatment would remain available to patients.). Recently, Essential Inventions, Inc., a non-profit organization, petitioned the government to receive licenses on Norvir® (Abbott Labs) and Xalatan® (Pfizer). Petitions cited the need to receive the licenses by demonstrating abusive pricing practices by the companies. For example, one of the petitions demonstrated how the price on Norvir® (Retinavir) was increased by Abbott 400% in a single day forcing consumers to buy a combination drug, which also included Norvir®, rather than two drugs separately. The NIH rejected these petitions, suggesting that "march in" provisions were not intended to control prices, and that additional legislation is required in this area. *See* Essential Innovations, Inc., *Petition to Use Authority Under Bayh-Dole Act to Promote Access to Latanoprost*, http://www.essentialinventions.org/legal (Jan. 29, 2004); Essential Innovations, Inc., *Petition to Use Authority Under Bayh-Dole Act to Promote Access to Ritonavir*, http://www.essentialinventions.org/legal (Jan. 29, 2004); *see generally*, Bonnie

Hatch-Waxman Act,[54] which codified the decision of the Federal Circuit allowing generic drug manufacturers to use a patented drug solely for the purpose of collecting information required for the drug approval process.[55]

The U.S. Government can also mandate a compulsory license by taking patented inventions through eminent domain.[56] Through eminent domain, the government breaks the patent monopoly, but the patent owner is allowed to seek damages in a private lawsuit against the federal government.[57]

Unlike the U.S. practice, a number of other countries require compulsory licenses for unused or misused pharmaceutical inventions.[58] Compulsory licensing is expressly authorized under TRIPS,[59] albeit in limited circumstances, and the World Trade Organization has upheld the validity of the Canadian equivalent of the "Bolar exception."[60]

The compulsory licensing mechanism works as a negative control rather than by positive reinforcement. Similar to decreasing the scope of claims, it is helpful in deterring abusive practices.[61]

Joy Sedlak, *National Institutes of Health Decides Not to March In: Exploring the Decision Reached in the Case of Abbott's Norvir*, 24 Genetic Engr. News 1 (Sept. 1, 2004); *see also* David Filmore, *Can Generics "March In ?"*, Modern Drug Discovery 49 (May 2004).

54 *Drug Price Competition and Patent Term Restoration Act of 1984*, Pub. L. No. 98-417, 98 Stat. 1585 (1984) [hereinafter *Hatch-Waxman Act*] (codified as amended in scattered sections of 15 U.S.C., 21 U.S.C., 28 U.S.C., and 35 U.S.C.) (creating, *inter alia*, 35 U.S.C. § 271(e)(1)); *see generally* Adi Gillat, *Compulsory Licensing to Regulated Licensing: Effects on the Conflict Between Innovation and Access in The Pharmaceutical Industry*, 58 Food & Drug L. J. 711, 714 (2003).

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

56 Thomas F. Cotter, *Do Federal Uses of Intellectual Property Implicate the Fifth Amendment?*, 50 Fla. L. Rev. 529, 541 (1998).

57 28 U.S.C. § 1498(a) (2000).

58 *See generally* Gianna Julian-Arnold, *International Compulsory Licensing: The Rationals and the Reality*, 33 IDEA 349, 372-95 (1993).

59 Gillat, *supra* n. 54, at 736 (citing *Agreement on Trade-Related Aspects of Intellectual Property Rights* pt. 2, § 5, art. 31(a)-(b) (Apr. 15, 1994) http://www.wto.org/english/docs_e/legal_e/27-trips.pdf).

60 *Id*. at 720.

61 *See* Kurt N. Saunders, *Patent Nonuse and the Role of Public Interest as a Deterrent to Technology Suppression*, 15 Harv. J. L. & Tech. 389 (2002); *see generally* Black, *supra* n. 45, at 397 (discussing reach-throughs).

3. Role of Regulatory Input

The pharmaceutical industry cannot be left entirely to market forces. Although our society assigns a high value to human life and dignity, firms cannot always account for societal costs or benefits[62] because they have an obligation to optimize returns to shareholders. Firms often optimize profits by selecting projects with both low risk and high expected return;[63] developing novel drugs for rare diseases is often neither low risk nor high return. The government should be able to implement risk-sensitive patent rewards to motivate firms to invest in developing medicines for areas of humanitarian need. *Ex post facto* rewards should be granted in proportion to investment-based risks.

B. Risks for the Three Industrial Segments

This article divides the pharmaceutical industry into three sectors for risk analysis: (I) large firms; (II) small firms; and (III) non-profit institutions.[64] Non-profit institutions are registered as such. It is a more complex task to divide a continuum of commercial firms into small and large entities. For simplicity,[65] this article divides commercial firms into small firms and large firms based on market cap or total sales, following the model presented in MIT's Magazine of Innovation Technology Review.[66]

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62 Societal benefits may include reduction in premature death, disability, pain and suffering, loss of consortium. A loss of these benefits are recognized as damages recognized by the American legal system. *See* Louis Kaplow, *The Patent-Antitrust Intersection: A Reappraisal*, 97 Harv. L. Rev. 1813, 1855-67 (1984) (discussing a detailed economic treatment of net societal benefits).

63 *See* Joseph A. DiMasi, Erol Caglarcan & Maria Wood-Armany, *Emerging Role of Pharmaeconomics in the Research and Development Decision-Making Process*, 19 (7) Pharmacoeconomics 753, 754 (2001).

64 This article focuses mainly on academic research institutions, although substantial research is conducted in hospitals, specialized research institutions and research foundations.

65 Administrative convenience favors classification created by the Small Business Administration, because firms certify qualification for "small entity" status during patent examination process. *See* 13 C.F.R. §§ 121.801-12.805 (2006); DiMasi, n. 63, at 755 (suggesting classification based on total investment into R&D; and total sales).

66 Mass. Inst. Tech., *Introducing the Technology Review Index: Keeping an Eye on Business*, Tech. Rev. 46, 46 (Mar. 2005) (reporting that large firms have an average market cap of $103 billon while small companies have an average market cap of $1.8 billion); *see also* Mass. Inst. Tech., *Data Mine: The Vitality of Biotech*, Tech. Rev. 86 (Jan. 2005) (reporting total yearly sales of $29 and $2 billion respectively. The 2003 revenues for top ten pharmaceutical firms ranged between ~$45 and $19 billon, and biotechnology firms ranged between ~$8 and $0.3 billon).

1. Industry Perspective

A firm may evaluate the risk of developing any particular drug as a ratio of expected drug development costs to the firm's total annual sales. The total annual sales reflect the ability of a firm to support the development of the drug. In the cases of companies which have minimal or no annual sales (such as non-profit institutions or start-ups), the market cap should be used instead. With the widely varying data and the lack of transparency in the pharmaceutical industry,[67] it is difficult to quantify risks.

a. Risks to Large Firms

This article uses the risk level of large pharmaceutical firms as the baseline for comparison with the other industry segments. Most novel drugs are developed by large firms; such firms can support the steep development costs.[68] The designation as baseline is justified by the high costs of drug development and substantial technical risks that remain throughout the development process.[69]

Industry proponents report that large firms bear the full costs of bringing a drug to market,[70] estimated to be between $500 million — $1.7 billion.[71]

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67 *See* Public Citizen, *supra* n. 4, at 10-11 (asserting that the industry has largely kept its research and development costs obscure).

68 Joseph A. DiMasi, *New Drug Innovation and Pharmaceutical Industry Structure: Trends in the Output of Pharmaceutical Firms*, 34 Drug Info. J. 1169, 1177 (2000).

69 Joseph A. DiMasi, *Risk, Regulation, and Rewards in New Drug Development in the United States*, 19 Reg. Toxicology & Pharmacology 228, 228 (1994).

70 *Id.* As one source comments:

> In 1999, the National Institutes of Health investigated whether its research funding commonly leads to the development of new drugs, the profits from which taxpayers might be entitled to share. Of 47 drugs that had earned revenues of $500 million or more, NIH support had figured significantly in only four.

Henry I. Miller, *Bookshelf: Fighting Disease Is Only Half the Battle*, Wall St. J. D10 (Aug. 25, 2004).

71 *See* Joseph A DiMasi, Ronald W. Hansen, & Henry G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. Health Econ. 151 (Mar. 2003); Kaitin K.I., ed., *Post-approval R&D Raises Total Drug Development Costs to $897 Million*, 5(3) Tufts Ctr. for Study Drug Dev. Impact Rep. (May/Jun 2003); *see also* Ann M. Thayer, *Blockbuster Model Breaking Down*, Modern Drug Discovery 23 (June 2004) (citing Bain and Company "Factoring in failed dug candidates, it calculates the costs of discovering, developing, and launching a single new drug at nearly $1.7 billion."); Tufts Ctr. for Study of Drug Dev., *Tufts Center for the Study of Drug Development Pegs Cost of a New Prescription Medicine at*

The firms must bring in sufficient revenue in sales to recoup costs and set aside funds for future research. It is reported that the pharmaceutical industry's fixed research and development cost is roughly 21% of total sales.[72] Since complete development of a new drug requires approximately 10 years, the percentage of sales necessary to cover costs is actually closer to 30% when the interest that would have accrued during development is taken into account.[73] Private sector investment into pharmaceutical development amounted to $26.4 billion in 2000,[74] with 17.5% of this going to the top 20 firms.[75] Firms argue that strong intellectual property protection is necessary to support continued pharmaceutical development and the survival of the industry.[76]

A report by the non-profit consumer protection group Public Citizen denies that large firms carry the full costs of drug development. It reported that 55% of all published research behind approved drugs was conducted in academic settings, and the overall public investment exceeded $20.3 billon in the year 2000.[77]

Public Citizen also disputes the estimated drug development costs, pointing out that the estimates focus exclusively on novel and consequently the most expensive drugs, while most of the drugs reaching the market are copycat drugs or reformulations.[78] It also points out that the numbers do not correlate with estimates from the industry's own lobbying group, Pharmaceutical Research and Manufacturers of America, nor estimates from the congressional Office of Technology Assessment.[79] The Public Citizen's report calculates a total development cost range between $67 and $100 million for an average drug.[80] Another source also suggests that the pharmaceutical industry artificially

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$802 Million, http://csdd.tufts.edu/newsevents/recentnews.asp?newsid=6 (Nov. 30, 2001) (explaining that the cost includes the sunk R&D costs for failed drugs).

72 Patricia M. Danzon, *Making Sense of Drug Prices*, 23 Reg. 56, 56-63 (No. 1 2000); *but see* Mass. Inst. Tech., *supra* n. 66, at 86 (reporting for the year 2003 an average R&D costs as a percent of revenue for top 10 pharmaceutical companies at 13% and for top 10 biotechnology companies at 29%).

73 Danzon, *supra* n. 72, at 56-63.

74 United Nations Development Programme & Sakiko Fukuda-Parr, *Human Development Report 2001* (Oxford U. Press 2001).

75 Pharmaprojects, *Annual Review* (2001).

76 Alan F. Holmer, *Opposing View: Drug Firms Conduct Valuable Research; Makers of Generics Do Not*, USA Today 14A (Oct. 29, 2001).

77 Public Citizen, *supra* n. 4, at 7-10 (detailing a review of taxpayers' contribution).

78 *Id.* at 7 (detailing the analysis of the development of copycat drugs versus novel drugs).

79 *Id.* at 1-2.

80 *Id.* at 3-4.

inflates reported research and development costs by including costs of administration and marketing.[81] Yet, the report admits that the costs of novel drug development for a complex disease can often exceed $500 million.[82]

Public Citizen also suggests that the U.S. pharmaceutical industry is extremely profitable[83] and should operate on a lower margin of profit.[84] Furthermore, low cost copycat projects, as opposed to high risk novel developments, are favored by large commercial investors.[85]

The drug development project, however, is multifaceted and usually only large firms have the capacity to carry out the later stages of the development and production.[86] Besides studying disease processes, firms must also identify potential new drugs and perform the laboratory and clinical testing to

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81 Marcia Angell, *The Pharmaceutical Industry – To Whom Is It Accountable?*, 342 New Eng. J. Med. 15304 (2000); *see also* Special Committee on Aging, U.S. Senate, The Drug Manufacturing Industry: A Prescription for Profits (Sept. 1991); *but see* Richard A. Epstein, *Pharma Furor: Why Two High Profile Attacks on Big Drug Companies Flunk the Test of Basic Economics*, Leg. Affairs 56, 56 (2005).

82 *See* Tufts Ctr. for Study of Drug Dev., *supra* n. 71 (updating the estimate upward of $800 million); Public Citizen, *supra* n. 4, at 5.

83 The Public Citizen comments:

> The 11 drug companies that made the Fortune 500 enjoyed 19 percent return on revenues . . . [t]he median for all other Fortune 500 companies was 5 percent return on revenues . . . [s]ince 1982, the industry has topped Fortune's rankings for return on revenues, has been at or need top for return on equity.

Public Citizen, *supra* n. 4, at 11-12. Another source comments:

> Over a longer span of time, economic returns to the pharmaceutical industry as whole exceeded returns to corporations in other industries by about 2 to 3 percentage points per year from 1967 to 1987, after adjusting for differences in risk among industries.

U.S. Congress, Off. Tech. Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards* 2 (U.S. Govt. Prtg. Off. 1993) (available at http://www.wws.princeton.edu/ota/disk1/1993/9336/9336.PDF).

84 Public Citizen, *supra* n. 4, at 11-12 (looking exclusively at pharmaceutical firms that made Fortune 500 list and ignoring small firms).

85 *See generally* Ma & Zemmel, *supra* n. 6 (discussing the prevalence of me-too drugs).

86 *See* Charles Dormer, *Fostering Innovation*, Modern Drug Discovery 17 (Nov. 2004); s*ee also StemCells Completes Equity Financing; $22.5 Million in Funds to Support Batten's Trial*, Bus. Wire (Nov. 1, 2004) (reporting that after completing the private placement of its shares, StemCells, Inc. has raised sufficient funds to take a drug candidate through Phase I trials. Impliedly, funds are not sufficient for Phases II and III, which are needed for drug approval.).

confirm the efficacy and safety of the drugs.[87] These activities require expensive reagents, specialized equipment, highly trained personnel with very different specialties, and a continuous incorporation of new technologies.

Also, pharmaceutical development is becoming increasingly expensive. Any drug may fail at any stage of development.[88] A widely quoted figure is that only 1 in 5000 leads is expected to yield a clinically approved product.[89] Many of the illnesses now being targeted by companies, such as cancer and asthma, are extremely complex and poorly understood[90] and there are few diseases remaining for which "simple" treatments can be found.[91] As traditional methods of drug discovery become less productive, the industry must invest heavily into risky new technologies.

Drug development is unquestionably a risky enterprise. Assuming that these risks to large firms are adequately compensated by the current level of patent rewards, this article uses large firms as a baseline for comparison of risks undertaken by small firms and non-profit organizations.

b. Risks to Small Firms

Small firms incur higher out-of-pocket and capitalized costs of drug development than large firms.[92] By definition, the value of a small firm will always be smaller than the value of a large firm. If the firm evaluates its ability to bring the drug to market as the ratio of projected drug development costs to the firm's value, the risk to a small firm will always be greater than the risk to a large firm. For the development of any given drug, the risk that a small firm

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87 Dormer, *supra* n. 86, at 18 (commenting that "Wyeth has developed a model it used to determine what is required to deliver 12 development track candidates per year — namely about 160 teams working at various stages of the project.").

88 DiMasi, supra n. 7, at 297; *see also* Danzon, *supra* n. 72, at 56-63; Jeanne Whalen, *Glaxo to Report on Many Drug Trials*, Wall St. J B2 (Feb. 10, 2005) (commenting that "only about 30% of drugs in Phase II ever make it to market . . . [a]bout 70% of drugs in Phase III trials eventually make it to market.").

89 H.R. Subcomm. On Intell. Prop. & Jud. Administration Comm. On Commerce, *Hearing on H.R. 4894 and S. 2368, General Agreement on Tariffs and Trade: Intellectual Property Provisions*, 103d Cong. 296 (1994) (statement of Gerald J. Mossinghoff, President, Pharmaceutical Research and Manufacturers of America).

90 *See* Joseph A. DiMasi, *New Drug Development in the United States from 1963 to 1999*, 69 Clinical Pharmacology & Therapeutics 286, 289-94 (No. 5, 2001) (showing variability in the success rate per therapeutic class).

91 Lansbury, *supra* n. 1, at S51.

92 Joseph A. Dimasi, Henry G. Grabowski & John Vernon, *R&D Costs, Innovative Output and Firm Size in the Pharmaceutical Industry*, 2 Intl. J. Econs. Bus. 201, 210-11 (No. 2, 1995).

would exhaust available resources is at least ten times greater than the risk to a large firm.[93]

Small firms invest more aggressively than large firms[94] by investing into the earlier and riskier stages of the development.[95] Thus, most innovative developments tend to come from small firms.[96] The expensive and time consuming drug development process, however, ties up a greater proportion of a small firm's resources. For the year 2003, average research and development costs as

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93 Joseph A. DiMasi, *Risk, Regulation, and Rewards in New Drug Development in the United States*, 19 Reg. Toxicology & Pharmacology 228-31 (1994) ("For small firms the risk can be that of survival in any form . . . . In the case of a start-up biotech firm where the availability of funds may, at some points in time, be significantly restricted, the firm may not survive a string of commercial or clinical failures."); *See also* DiMasi, *supra* n. 71, at 151 (estimating the market cap and sales for small firms). Also, two pharmaceutical companies in top ten venture capital deals in 2004 secured $250 million and $80, short of estimated $800 million drug development costs. *See Private Markets*, MIT's Mag. Innovation Tech. Rev. 38 (Mar. 2005). Similarly, two pharmaceutical companies in top ten IPO's in 2004 raised only $137 and $45 million. *Id.* at 40.

94 *Financing the Biotech Industry: Can the Risks Be Reduced?*, 4 B.U. J. Sci. & Tech. L. 1, 19 [hereinafter *Financing the Biotech Industry*] (quoting Stanley Erck, "I marvel at the number of people who will start biotechnology companies. It is a unique industry, in my view, because you have to be willing to start a company that will not produce sales from real products for a minimum of ten, and often fifteen years."); *See also* Joe Alper, *Biotech Thinking Comes to Academic Medical Centers*, 299 Science 1303 (2003) (quoting "Risk is the birthright of start-up biotech companies . . . . Only 10% of the compounds pass the preclinical stage and more than 80% fail in clinical trials."); *See* Michael Malinowski & Maureen O'Rourke, *A False Start?*, *The Impact of Federal Policy on the Genotechnology Industry*, 13 Yale J. On Reg. 163, 206-08 (1996).

95 C. Boyd Clark, *Big Pharma? Think Again*, Wall. St. J. B2 (Oct. 12, 2004) ("[M]ore than 90% of [small] companies remain unprofitable 30 years into biotech age. Most are posting hefty net losses - $9 billion total in 2002."); *see also* Richard A. Mann, Michael O'Sullivan, Larry Robbins & Barry S. Roberts, *Starting From Scratch: A Lawyer's Guide To Representing A Start-Up Company*, 56 Ark. L. Rev. 773 (2004) (citing Thomas Zimmerer & Norman M. Scarborough, *Essentials of Entrepreneurship & Small Business Management* 10 (3d ed., Prentice Hall 2002) "[m]ost of these businesses are not long term survivors: 24% of new businesses fail within two years while 63% fail within six years."); s*ee e.g.* Antonio Regalado, *U.S. Pair Gets Nobel Medicine Prize*, Wall St. J. A8 (Oct. 5, 2004) (describing that although at the moment there is no market for the award winning technology, Sentigen Holding Corp. has licensed it from Columbia University and obtained a federal grant to support development).

96 C. Boyd Clark, *supra* n. 95, at B2 ("biotech has brought almost 200 medicines into the marketplace."); *see also* John R. Allison et al., *Valuable Patents*, 1, 42 (2003) (available at http://papers.ssrn.com/abstract=426020) ("The first possible interpretation is that small rather than large entities are the real wellsprings of innovation in the United States."); *but see* Joseph A. Dimasi, Henry G. Grabowski & John Vernon, *supra* n. 92, at 215 (1995) (suggesting that large firms are the most innovative).

a percent of revenue was 13% for the top ten large pharmaceutical firms and 29% for the top ten small biotech firms.[97] Phase III clinical trials account for roughly half of the total cost of bringing a drug to market and it is not uncommon for costs to run over a million dollars per patient.[98] The government provides grants and loans through the Small Business Administration and the National Institutes of Health (NIH),[99] but small firms still often lack the resources to bring drugs all the way to market[100] without an exclusive agreement or buyout arrangement with a large firm.[101]

This article suggests that in proportion to large firms, small firms take higher risks and consequently are not sufficiently rewarded by the current patent reward level.

c. Risks to Non-Profit Institutions

Universities should not be given preferential treatment solely on the basis of their non-profit status. Although we sometimes treat universities as idealistic philanthropic institutions, the reality of the 21st Century makes them businesses.[102] In most developed nations today, universities conduct between 15 and 20% of all pharmaceutical research and development, while the public sector accounts for another 10-15%.[103] The courts recognize this fact and decline to

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97 *See* Mass. Inst. Tech., *supra* n. 66, at 86 (noting that biotechnology firms represent small firms in the pharmaceutical industry).

98 Lansbury, *supra* n. 1, at S54.

99 Josh Lerner, *The Government as Venture Capitalist: The Long-Run Impact of the SBIR Program* (Feb. 1998) (available at http://ssrn.com/abstract=4746); *see* Gwendolyn Bounds, *Fed Funds: A Guide to SBA Lending Programs*, Wall St. J. R8 (Nov. 20, 2004) (showing a detailed analysis of available funds); *see also* Gwendolyn Bounds, *The Great Money Hunt: Financing is a Life Boat for Small Firms. But How do You Know How Much You Need? And Where Can You Go to Get It*, Wall St. J. R1 (Nov. 20, 2004).

100 *See* Mass. Inst. Tech., *supra* n. 66, at 86 (reporting that the number of deals between biotech and pharmaceutical firms has steadily increased reaching ~750 in 2003-04); *see also* DiMasi, *supra* n. 68, at 1177 (reporting that the proportion of FDA filings for self-originated drugs to licensed-in drugs has declined more than 10% from the 1960's to the 1990's.).

101 *Deals*, Modern Drug Discovery 19 (Apr. 2004) (noting Genzyme's acquisition of ILEX Oncology, Inc. for $1 billion dollars and a bid to acquire IMPATH for $215 million, Merck's agreement to acquire Aton Pharma, Inc. and Fisher's acquisition of Oxoid for $80 million.).

102 Bernard Wysocki Jr, *Columbia's Pursuit of Patent Riches Angers Companies, As University Seeks to Extend A $600 Million Bonanza, Biotechs Refuse to Pay Up*, Wall St. J. A1 (Dec. 21, 2004); *see also* Bernard Wysocki Jr, *Business School: How Dr. Papadakis Runs A University Like A Company*, Wall St. J. A1 (Feb. 23, 2005).

103 DiMasi, s*upra* n. 63, at 755.

exempt universities from the scrutiny of antitrust[104] and intellectual property laws.[105]

Prior to 1980, inventions developed with public funds could not be patented and thus were available to everyone. The passage of the Bayh-Dole Act in 1980 allowed non-profit organizations to obtain patents.[106] This Act was intended to stimulate productivity by encouraging the commercialization of new inventions.[107] The Act, however, may not have produced the expected level of results.[108] Although it has increased revenue to universities,[109] this may merely reflect the acquisition of previously prohibited patents rather than new scientific discoveries or commercialization. Additionally, several studies warn of the dangers of reducing the free exchange of information traditionally found in academic settings.[110]

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104 *U.S. v. Brown U.*, 5 F.3d 658, 666 (3d Cir. 1993) ("The exchange of money for services, even by a nonprofit organization, is a quintessential commercial transaction.").

105 *Madey*, 307 F.3d at 1359; *see also* Bernard Wysocki, Jr., *Cutting Edge: A Laser Case Sears Universities' Rights To Ignore Patents*, Wall Street J A1 (Oct. 11, 2004).

106 *The Bayh-Dole Act*, Pub. L. No. 96-517, 94 Stat. 3015 (1980) (codified as 35 U.S.C. §§ 200-211).

107 *See* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 Science 698 (1998).

108 Lansbury, *supra* n. 1, at S53 ("Although [the Bayh-Dole Act] has resulted in the proliferation of university technology transfer groups and startup biotechnology companies, the steady reduction in the rate of approval of new drugs over the past 10 years argues that it has impeded progress."); Peter T. Lansbury, Jr., *In Support of NIH's Road Map*, 83(2) Chem. & Engr. News 4 (Jan. 10, 2005) ("[the] gap between what we know about human biology and what we can offer patients has never been larger [and] the rate of introduction of novel medicines has been decreasing steadily.").

109 Sen. Subcomm. On Pats., Copys., & Trademarks of the Comm. on Jud., *Hearing on Pub. L. No. 96-517, The Bayh-Dole Act, A Review of Patent Issues in Federally Funded Research*, 103d Cong., 2nd Sess., 1-2 (1994); *see also* Shira Boss-Bicak, *Moving Ideas Off Campus: Research Projects Graduate From University to Marketplace*, NY Times C6 (Oct. 28, 2004) (asserting that the revenue to universities nearly doubled to $1.3 billion between 1997 and 2002 while the number of patents increased to 3,600 in 2002).

110 Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 Va. L. Rev. 1663, 1698, 1715 (1996), [hereinafter *Public Research and Private Development*] ("There is a fine line between using patents to motivate universities to cooperate in transferring research discoveries to the private sector for commercial development and using patents to motivate universities to perform research of a character that is likely to yield potential commercial products."); *see also* Barry Meier, *Contracts Keep Drug Research Out of Reach*, NY Times A1 (Nov. 29, 2004); *see also* Wysocki, *supra* n. 102, at A1 (citing studies of Arti Rai, Duke U., Rebecca S. Eisenberg, U. of Mich. & John Thomas, Georgetown U.).

Non-profit institutions are not under pressure to produce commercial returns and so are free to pursue fundamental research. Patent grants for such research tend to be broad, often preventing other parties from developing that technology. This leads to a higher potential for technology suppression[111] because non-profit institutions usually are ill equipped to bring their products to market.[112] If the inventions are transferred or licensed to commercial entities for further development, these entities often charge supra-competitive prices,[113] thus free-riding on publicly funded research. The total benefit to the public is unclear.[114] Essentially, the public pays twice: once when investing into drug research and development in the non-profit setting, and again when paying for the drug on the market.[115]

It is difficult to estimate investment risks for non-profit institutions. These institutions carry only partial drug development costs because academic discoveries are usually confined to the early stage of development.[116] Furthermore, these costs do not reside with the institutions because of their publicly funded nature. As a result, the monetary risk to non-profit institutions is, in substance, zero. While there is some risk to reputations and careers of academic scientists, this does not differ from the risks to scientists in commercial firms. In the comparative analysis of this article, the non-monetary risks cancel out.

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111 *See* Heller & Eisenberg, *supra* n. 107, at 698 ("[a] proliferation of intellectual property rights . . . may be stifling life-saving innovations . . ." due to the blocking occurring when too many owners hold the right in parts necessary for completing the whole product.); *see also supra* n. 44-46, 53 and accompanying text.

112 *See* Ann Grimes, *Why Stanford Is Celebrating The Google IPO*, Wall St. J. B1 (Aug. 23, 2004) (noting that technology licensing carries high transaction costs. The university licensing offices use 15% of total revenue collected.).

113 Randall C. Willis, *The Price is Right? For Pharmaceuticals, It's Not Just the Costs, It's the Market*, Modern Drug Discovery 23 (Feb. 2004).

114 *See Public Citizen Health Research Group v. NIH*, 209 F. Supp. 2d 37 (D.C. D.C. 2002) (noting that the total return was unclear, as NIH refused to release royalty information for both intramural inventions and inventions made under cooperative research and development agreements. The right to withhold information was affirmed by the U.S. District Court for the District of Columbia.).

115 Arguably, the goal of promoting new drugs for understudied diseases of complex biology is better served by allowing large firms to reap supracompetitive profits delivered by academia "on a silver platter." *See* Alper, *supra* n. 94, at 1303 (citing Stein "We want to hand potential drugs to the pharmaceutical industry on a silver platter"); *see also* Minkel, *supra* n. 8, at 24 (arguing that it is possible that the drugs would be brought to the market in the most expedient matter, when most of the high risk research is completed in academia. This view maybe shortsighted and the societal costs may become prohibitive, if the delivery of profits would not be accompanied by redistribution of resources.).

116 Lansbury, *supra* n. 1, at S54; *see also* Alper, *supra* n. 94, at 1303.

Therefore, in relation to commercial firms, non-profit organizations are over-rewarded by the current patent reward level.

2. Investor Perspective

Another model looks at the ability of a firm to deliver desired returns to investors.[117] Investors invest into large pharmaceutical firms when stable long term investments are desirable.[118] Large firms endeavor to ensure their long-term survival by supporting multiple projects simultaneously.[119] The standard financial models for investments predict that most diversifiable risk is eliminated in a portfolio of ten securities,[120] "while a portfolio of size 20 eliminates 95% . . . of the diversifiable variance."[121] By analogy, large firms carry little diversifiable risk, as illustrated by the fact that all of the top ten pharmaceutical firms carry more than 20 projects simultaneously.[122] Large firms further ensure the ability to deliver expected returns by carrying a portfolio of generic drugs[123] or investing into off-shore research and development.[124]

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117 DiMasi, *supra* n. 93, at 229-30 (1994) (acknowledging that although investors can diversify risks, the concern is great for investors concentrating holdings in a few firms, and that not all risks are diversifiable.).

118 Public Citizen, *supra* n. 4, at 12 (noting that "[t]he drug industry often thrives when other industries sag"); *see* James B. Stewart, *After Shock of Vioxx, Diversification Is Key To Investing In Drugs*, Wall St. J. D5 (Oct. 6, 2004); Gautam Naik, *Elan's Ups and Downs Continue*, Wall St. J. B3 (Mar. 2, 2005) (arguing that while the benefit of diversification within the large firm provides security to the investor as a general principle, the recent withdraw of Vioxx by Merck and troubles of Elan may cast a doubt on sectors stability.).

119 Charles Dormer, *Fostering Innovation*, Modern Drug Discovery 17, 18 (Nov. 2004) ("Wyeth Discovery has produced 12 development track compounds per year for the past three years [since 2001], up from an average of just three compounds per year in the 1990s)"; *see also* Jeanne Whalen, *Glaxo to Report on Many Drug Trials*, Wall St. J B2 (Feb. 10, 2005) ("Half of the 90 new medicines Glaxo is testing are only midway through the development process.").

120 John L. Evans & Stephen H. Archer, *Diversification and the Reduction of Dispersion: An Empirical Analysis*, 23 J. Fin. 761, 761-67 (1968).

121 James M. Park & Jeremy C. Staum, *Diversification: How Much is Enough*, SSRN, Paper No. 85428.

122 DiMasi, *supra* n. 68, at 1177, tbl. 2.

123 *See* Jeanne Whalen, *Novartis Expands Generics Range for $8.4 Billion: Acquisition of Two Firms Aims at Growing Demand for Broader Drug Portfolio*, Wall St. J. A1 (Feb. 22, 2005) (describing the acquisition of two generic drug manufacturers by Novartis); *see also* Jeanne Whalen and Leila Abboud, *Big Pharma, Flush with Cash, Is Looking Acquisitive*, Wall St. J. C1 (Feb. 16, 2005).

124 Laura Santini, *Drug Companies Look to China For Cheap R&D*, Wall St. J. B1 (Nov. 22, 2004).

In contrast, small firms obtain suboptimal diversification benefits[125] because their limited resources cannot maintain investment into more than a few projects at a time.[126] Small firms can only focus on a few drug candidates at a time although they may have several promising leads.[127] Furthermore, small firms are riskier for stock investors because the costs of capital are higher for small firms.[128] To offset the higher costs of capital, small firms need to deliver higher expected returns.[129]

The risks of non-profit institutions are well diversified. Traditional funding for non-profit institutions comes from public grants.[130] The overall investment is typically large,[131] and the risk is spread over a large number of projects. Thus, the investment risk to each individual society member is small.[132]

Since scientific groups work in relative isolation,[133] their individual abilities to produce results are not spread over other publicly funded projects within a non-profit institution.[134] This does not matter to the public, however, because the public invests in all the projects.[135]

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125 *See supra* n. 120-121 (setting optimal diversification benefits at the portfolio of 10 to 20 securities (projects)).

126 *See e.g.* Amy D. Marcus, *A Patient's Quest to Save New Drug Hits Market Reality*, Wall St. J. A1, A17 (Nov. 16, 2004) (describing Titan Pharmaceutical, a small company with fewer than 100 employees and 6 drugs in various stages of testing (only two of which were in late stages prior to withdraw of TriAb from trials). The company founded in 1993, still does not have a product on the market.).

127 *Id.*

128 Joseph A. DiMasi, *supra* n. 93, at 230.

129 *Id.*

130 *See* Sharon Begley, *Anxious for Cures, Grant Givers Turn More Demanding: To Speed Discovery Process, Scientists Must Share Data As Condition for Funding*, Wall St. J. A1 (Sept. 29, 2004).

131 Jason Pontin*, The Crisis in Tech Finance*, MIT's Mag. Innovation Tech. Rev. 10 (Mar. 2005) ("[i]n the 2005 federal budget, R&D spending has increased 4.8 percent to $132.2 billion . . . . National Institute of Health . . . R&D budget increase[d] . . . to $27.5 billion . . . .").

132 Investment through taxation is directed to an overall improvement in the quality of life, which is difficult to compare with traditional commercial investment. The decisions on investment value and allocation do not reside with individual investors, but are delegated to review boards assigned by the government. Investment into pharmaceutical development is only a small portion of the overall "quality of life" investment through taxation.

133 Lansbury, *supra* n. 108, at 4.

134 *Id.*

135 *Id.*; *see also* Sharon Begley, *Anxious for Cures, Grant Givers Turn More Demanding*, Wall St. J. A1 (Sept. 29, 2004).

In summary, both large firms and non-profit institutions more fully diversify risks, while small firms obtain only sub optimal diversification. Consequently, small firms carry higher risks for investors and are under-rewarded by current patent rewards.

3. Employee Perspective

Risks from an employee's perspective include the risks of decreased salary or of losing employment when drug development fails. Employees of large firms enjoy greater security because the failure of a single drug in development would not be likely to bankrupt the firm.[136] The employees are often redistributed from failed projects to remaining projects.[137] In contrast, the employees of small firms are at constant risk and the failure of a major project may often result in the loss of jobs.[138]

Academia provides secure employment for tenured researchers. However, non-tenured professors and research associates whose salaries are derived from grants may have more precarious positions.

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136 *See* Gautam Naik, *Elan's Ups and Downs Continue*, Wall St. J. B3 (Mar. 2, 2005) (Stating that the stock of Elan Corporation crashed following the withdrawal of the Alzheimer vaccine from Stage III clinical trials (from ~$45/share to ~$2) in 2002. The stock crashed again in 2005, following the withdrawal of Tysabri, a drug for multiple sclerosis (from ~$28/share to ~$8/share)).

137 *See e.g.* Scott Hensley, *Pfizer Plans $2 Billion in Cost Cuts*, Wall St. J. A3 (Feb. 11, 2005) (describing how Pfizer is planning on reorganization to allow for $2 billion cost cuts without planning for widespread layoffs); *but see Bristol Carries Out Promised Job Cuts*, http://www.jobbankusa.com/News/Layoffs/layoffs111704a.html (Nov. 17, 2004) (describing lay-offs of 70 scientists, chemical engineers, etc).

138 For example, Maxim Pharma announced a 50 percent reduction in workforce less than one month after reporting a poor outcome for a lead compound in a Phase III clinical trial. Val B. Kennedy, *CBS Market Watch: Key drug setback for Maxim Pharma*, http://www.marketwatch.com/news/archivedStory.asp?archive=true&dist=ArchiveSplash&siteid=mktw&guid=%7BFF5D7FBB%2D1A1B%2D4F81%2DBA63%2D3A5F78C9A9FC%7D&returnURL=%2Fnews%2Fstory%2Easp%3Fguid%3D%7BFF5D7FBB%2D1A1B%2D4F81%2DBA63%2D3A5F78C9A9FC%7D%26siteid%3Dmktw%26dist%3D%26archive%3Dtrue%26param%3Darchive%26garden%3D%26minisite%3D (Nov. 1, 2004); *see also Tapestry Pharmaceuticals, Inc. (TPPH) Announces Plant to Discontinue Gene Editing Operations; Laying Off 20 Workers Or 25 Percent of Tapestry's Workforce*, http://www.biospace.com/news_story.cfm?StoryID=18174220&full=1&print=1 (Nov. 17, 2004); *see also Genta Cancer Drug Fails Late-Stage Trial*, http://reuters.com/printerFriendlyPopup.jhtml?type=topNews&storyID=6929148 (Nov. 26, 2004) (reporting 45 percent workforce reduction) (on file with author).

4. Summary of Risks Associated with Drug Development

Assuming that the investment-based risks undertaken by large firms are adequately compensated by the current level of patent rewards, this article proposes that small firms undertake greater risks and so should be better rewarded, while non-profit institutions undertake less risk and so are currently over-rewarded.

C. Expected Returns for the Three Different Drug Types

The next section evaluates expected returns in relation to the specific nature of the drugs in development: (a) novel drugs, (b) orphan drugs, and (c) copycat drugs. Novel drugs are new medicines used to treat diseases that affect large populations where the expected revenue justifies drug development costs.[139] Orphan drugs are medicines used to treat diseases that affect small populations ─ under 200,000 ─ patients where but for additional rewards from their development the projected revenue is not generally expected to recoup research and development costs.[140] Copycat drugs are medicines which provide only marginal new benefits because they are similar to existing drugs.

This article suggests that patent law should support projects that require higher investment per dollar of expected return. This inverse expectation value is loosely called 'risk' throughout the following sections of this article.

1. Novel Drugs

This article defines novel drugs as medicines for diseases that affect more than 200,000 patients, where the drug exploits a novel therapeutic mechanism.[141] Most novel drugs are developed by large firms, though some are ac-

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139 *See* Zachary Zimmerman, *Silence is Golden*, Bio-IT World 12 (Dec. 2004) (describing recently filed INDAs for the treatment of age-related macular degeneration from Acuity Pharmaceuticals and Sirna Therapeutics and imminent filings from Alnylam Pharmaceuticals. Companies enter into the field, where treatments already exist or in trials (from Eyetech and Genentech) but where entry marks the first use of RNA interference technology for patient treatment).

140 *See supra* n. 32 and accompanying text.

141 Novel drugs are distinguished from copycat drugs (*see supra* n. 4) and orphan drugs (*see supra* n. 32).

quired from small firms and non-profit institutions at a later stage in development.[142]

The current patent reward level is sufficient to stimulate the development of novel drugs. The FDA approved an average of 23 new molecular entities per year from 2000 to 2003.[143] This article uses the risk level associated with the development of novel drugs as a baseline because their development is economically feasible due to the high expected return on investment.[144]

An exception would be the case of novel blockbuster drugs, defined as such if the annual expected sales exceed $1 billion; these are likely to be developed even without assurances of exclusivity.[145] In these situations, patent incentives could be reduced in an attempt to encourage reallocation of resources towards other areas of needed research.

2. Orphan Drugs

The Orphan Drug Act classifies diseases that affect less than 200,000 patients as orphan.[146] Even within this category of diseases, the size of the patient pool and the quality of the statistics (e.g., poor diagnosis) affect the investment decisions of pharmaceutical firms.[147]

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142 *See* DiMasi, *supra* n. 68, at 1177.

143 *See Facing Our Demons*, 2 Nat. Revs: Drug Discovery 87 (Feb. 2003).

144 U.S. Congress, Off. Tech. Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards* 1 (1993) (available at http://www.wws.princeton.edu/ota/disk1/1993/9336/9336.PDF). Each new drug introduced to the U.S. market between 1981 and 1983 returned, net of taxes, at least $36 million more to its investors than was needed to pay off the R&D investment. The surplus return amounts to about 4.3 percent of the price of each drug over its product life. *Id.*

145 *See* Ann M. Thayer, *Blockbuster Model Breaking Down*, Modern Drug Discovery 23 (June 2004) (citing Graham Lewis, IMS vice president for strategic consulting, "[i]t's also significant that the number of blockbusters continues to grow, with 64 products having over $1 billion in sales in 2003, and 23 of those over $2 billion."); *see also* Nicholas Zamiska, *New Weight—Loss Drugs Are under Development*, Wall St. J. D6 (Oct. 5, 2004) (describing that more than 100 weight-loss medications are in the early stages of development, while a number of drugs is already on the market); *see also* Bruce Japsen, *Viagra's 2 Rivals Grab Market Share in a Year*, Chi. Trib. 3 (Sept. 23, 2004); *see also* Leila Abboud, *Ivax Takes Risk With the Launch Of Pfizer Copycat*, Wall St. J. D5 (Aug. 19, 2004) (describing Ivax binging neurotonin on the market prior to resolving a patent infringement suit).

146 *See supra* nn. 32-34 and accompanying text.

147 *See CuraGen Corporation (CRGN) Receives Orphan Drug Designation From The FDA For CR002 In IgA Nephropathy Indication* (Dec. 10, 2004) (available at http://rarediseases.about.com/b/a/131842.htm).

The Orphan Drug Act currently provides patent exclusivity extensions for orphan drugs.[148] This has been successful in stimulating the research and development of orphan drugs because drug development costs are prohibitively high compared to the expected returns. When the target market is small, companies are unlikely to risk investment into drug development without the promise of a monopoly. For example, the revenue from 100,000 patients paying $1000 a year for a drug would be unlikely to recoup research and development costs prior to patent expiration if extensions were not granted.[149] Increasing patent incentives for orphan drug development, especially for conditions affecting extremely small populations, can motivate more companies to invest into these currently under-researched areas.

3. Copycat Drugs

Copycat drugs are highly profitable and have limited technical risks associated with their development.[150] These sophisticated imitations carry low risk of failure because they are mostly created via low cost medicinal chemistry,[151] and their approval processes are also much cheaper and faster than those for novel drugs.[152]

Although copycat drugs deserve patent and regulatory protection,[153] the current level of patent rewards is extremely high in proportion to the develop-

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148 *See supra* n. 32 and accompanying text.

149 *See* DiMasi, *supra* n. 71, at 151 (providing $100 million in sales per year, when estimated costs of development exceed $800million). The remaining basic patent term rarely exceeds 5 years, as regulatory approval consumes 10-12 years. *See supra* n. 31 and accompanying text (noting that the industry has a tendency to patent early, long before engaging in regulatory approval process); *See also* David Armstrong, *Cancer Drug May Aid Young Leukemia Patients*, Wall St. J. D2 (Dec. 30, 2004) (showing a real example, Clolar, a leukemia drug from Genzyme Corp. The drug is expected to treat 500 to 1000 leukemia patients between ages 1 and 21 a year at a price tag of approximately $34,000 a dose. It is expected to gross about $100 million a year, as in this article's hypothetical example.).

150 Lansbury, *supra* n. 1, at S54; *See* Bruce Japsen, *Viagra's Two Rivals Grab Market Share in a Year*, Chi. Trib. 3 (Sept. 23, 2004) (highlighting some infamous copycat drugs which include Levitra marketed by GlaxoSmithKline and Bayer and Cialis from Lilly Icos, both designed to compete with Pfizer's Viagra).

151 Lansbury, *supra* n. 1, at S54 ("[i]t is profitable and not all that risky to generate new, patentable versions of existing drugs. So we have esomeprazole replacing omeprazole and deslortadine replacing lortadine. . . . [T]hese copycat drugs do not significantly benefit the public – albeit some have more favorable side-effect profiles.").

152 *See* 21 U.S.C. § 355(j) (1994) (Abbreviated New Drug Application (ANDA) provisions).

153 Richard A. Epstein, *Pharma Furor*, Legal Affairs 56, 57 (Jan.-Feb. 2005) ("Me-too drugs benefit health and safety because of [the] differences in patient's risk profiles. . . . [I]t may

ment costs. The investment into copycat drugs diverts funds away from other areas of needed research;[154] reducing patent incentives may redirect research efforts into other needed areas.

4. Summary of Expectations Associated with Different Types of Drugs

This article proposes that the current level of patent rewards for novel drugs is adequate because it is sufficient to motivate the continued development of these drugs despite high costs. Orphan drugs have much lower expected returns on investment because the target population is so small, and despite the Orphan Drug Act, their development is still mostly under-compensated by the current level of patent rewards. Copycat drugs, on the other hand, have much higher expected returns on investment, so are over-rewarded by the current level of patent rewards.

D. Relation Between the Industry Sectors and the Types of Drugs – Support Values (SV).

For comparative analysis, this article creates a number called the support value (SV) to indicate whether current patent rewards provide adequate compensation based on investment risks. A negative SV means that the enterprise is currently over-rewarded and thus, patent support should be decreased. A positive SV means that the current patent reward level is insufficient, and patent support should be increased in order to encourage investment into these areas.

The SV for large firms is set at baseline and assigned a value of zero because the high costs of drug development justify the current level of patent rewards. The patent rewards are sufficient and no further support is needed. As discussed in the previous sections, non-profit organizations have lower monetary risk and so and are assigned an SV of -1, implying that they are currently overcompensated by patent rewards and that the support can be decreased. Risks to small firms in comparison to large firms are higher and so are assigned an SV of +1, indicating the need for increased patent support.

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be acceptable to pull Vioxx off the market because patients . . . can switch to Celebrex and Bextra. Without me-too drugs, we put all eggs in one basket, which is always a dangerous strategy.").

[154] Lansbury, *supra* n. 1, at S54.

Expected returns associated with the development of novel drugs is set at baseline and assigned an SV of zero because their development is economically feasible even in the view of high costs, and the current level of patent support is adequate. Expected returns from copycat drugs are much higher, so the SV for copycat drugs is -1 to suggest that current support can be reduced. The expected returns from orphan drugs are lower than baseline, so the SV value is +1, indicating that these drugs require additional incentives to stimulate increased development.

The Support Value Addition Chart, below, is used to rank the support values of the different pharmaceutical entities in combination with the support values for the different types of drugs. The values on the chart are only a guide for comparison. They are not quantitative or proportional to the differences in risk and expectations; they also do not represent the probability of any of these situations occurring.

1. Support Values (SV) Chart

		Support Values for Different Pharmaceutical Entities		
		Non-Profit low SV = -1	**Large Firms** baseline SV = 0	**Small Firms** high SV = +1
Support Values for Different Drug Types	**Copycat** low SV = -1	lowest SV **-2**	**-1**	**0**
	Novel baseline SV = 0	**-1**	**0**	**+1**
	Orphan high SV = +1	**0**	**+1**	highest SV **+2**

A zero on the SV addition chart means that scenario yields a combined SV of zero. This baseline value indicates that the current patent rewards are adequate for the scenario and no further patent support is needed. A negative SV means that risks are lower and expected returns per dollar invested are higher than baseline, and therefore patent support may be decreased. A positive SV means that risks are higher and expected returns are lower than baseline, and therefore increased patent support is warranted. The scenarios will be described in detail in the following section.

III. PROPOSAL FOR RISK-SENSITIVE REWARDS

This article proposes making patent rewards proportional to risks and inversely proportional to expected returns as ranked by the support values in the chart. By altering patent incentives, this system may help guide pharmaceutical firms to redirect resources towards innovative research and socially desirable projects.

A. Patent Rewards at Initial Allocation

A non-profit institution developing a copycat drug yields a total SV of -2 on the SV chart. This is the least risky scenario on the chart and implies that the current level of patent rewards greatly over-compensates the risks, and thus the patent support can be decreased. The patent term can be reduced in proportion to the shorter time needed for development and regulatory approval; abbreviated new drug applications (ANDA) are usually processed and approved much faster than investigational new drug applications (INDA). Another mechanism for reducing the rewards may be royalty-free compulsory licensing, which can be applied to unused inventions or inventions used for blocking improvements.[155] The licensing can be administered without reducing initial commercialization incentives.[156] This scenario on the chart, however, may be only of theoretical interest, as non-profit organizations rarely develop copycat drugs. Bringing copycat drugs to market requires a large marketing and sales force that most non-profit institutions do not have.

A non-profit organization developing a novel drug yields an SV of -1 on the SV chart. A -1 indicates that the current level of patent support should be decreased; the lower risks and higher expected returns on investment in relation to the baseline results in overcompensation by the current level of rewards. The rewards granted to non-profit organizations can be reduced through compulsory licensing at reasonable market rates. Reducing the patent term, however, is disfavored because the pioneering inventions from non-profit institutions are usually confined to the early stages of development and may take a long time to commercialize.

A large firm developing a copycat drug also yields an SV of -1 on the chart. Most copycat drugs are introduced by large firms capable of bringing a competing drug to market dominated by the original drug. The rewards can be

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155 *See* Murdock & Fisher, *supra* n. 44, at 254.

156 The mechanism will not deter entities that are planning to bring a product to market, but will deter entities that acquire a patent for shelving.

adjusted by reducing the patent term either in proportion to the shorter time needed for regulatory approval[157] or by deducting a period equal to the extension period granted under Hatch-Waxman Act.[158] Reducing the scope of patent claims or implementing compulsory licensing mechanisms would be ineffective because patents for copycat drugs already have a narrow scope and the original drug, as well as any other competitors, already dominate the market.

The development of a novel drug by a large firm adds up to an SV of zero. Similarly, the SV values for non-profit institutions developing orphan drugs and small firms developing copycat drugs are also zero. Zero indicates a baseline level of risks and expectations and implies that the current levels of patent compensation are adequate. A small firm developing a copycat drug, however, is an unlikely scenario because copycat drugs require a large marketing and sales force that most small firms do not have.

There are two exceptions in this baseline SV group that should be assigned a SV of -1 due to their decreased need for support. First, blockbuster drugs, which are defined as drugs whose annual sales are expected to exceed $1 billion; these are likely to be developed even without assurances of exclusivity. Second, novel drugs developed with the assistance of public funding; these carry disproportionately lower risk because public funding divests investment risks while all the expected investment returns reside with the firm.[159] A decreased SV of -1 and the corresponding level of patent rewards would be more appropriate in these cases. Compulsory licensing at reasonable market rates would be the preferred mechanism for reducing rewards[160] in such situations.

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157 Abbreviated New Drug Applications (ANDA) used for copycat drugs are usually processed and approved much faster than Investigational New Drug Applications (INDA).

158 The proposed fixed reduction in patent term can be implemented with little administrative costs by differentiating filings of new drug applications from abbreviated new drug applications.

159 *See* Marilyn Chase, *Novartis Sets Deal To Seek New Drugs for Fighting TB*, Wall St. J. D9 (Oct. 27, 2004) (showing an example of a collaboration between Novartis and a non-profit organization Global Alliance for TB Drug Development); *see* Marilyn Chase, *Glaxo AIDS Drugs to Be Tested In Topical Form, as Microbicide*, Wall St. J. B3 (Sept. 24, 2004) (describing an example of collaboration between GlaxoSmithKline and a non-profit AIDS agency).

160 *See* Coe A. Bloomberg, *Federal Funded Inventions and Bayh-Dole Act Compliance: Do You Really Own What You Think You Own?*, 16(2) J. Proprietary Rights 1 (2004) (demonstrating that compulsory licensing is easy to administer because the revenue information and the information on public funding is readily available. Failure to mark the patent makes it unenforceable.).

The threat of compulsory licensing reduces incentives to abuse the patent,[161] while the ability to obtain such a license encourages the self-policing of the industry.

SV analysis for large firms developing orphan drugs yields an SV of +1 on the chart. This reflects higher risks and lower expected returns on investment in relation to the baseline. A positive SV indicates insufficient compensation by the current level of patent rewards and the need to increase this support in order to promote this scenario. Large firms need additional incentives to invest into the research and development of orphan drugs due to the low expected return on investment. Additional rewards may come in the form of an increase in the patent term, such as increasing the Hatch-Waxman Act extension, in addition to the extension provided through the Orphan Drug Act.

The situation of small firms developing novel drugs also yields an SV of +1. Small firms frequently invest in research and development of novel drugs[162] but take on higher proportional risk than do large firms because the total assets of small firms are so much smaller. Increasing patent rewards may enable them to attract more venture capital and facilitate the development and marketing of the final product.[163] Even when public grants help subsidize development costs, the high risk undertaken by small firms may justify higher rewards.[164] The rewards can be increased by extending the monopoly term, for example, by doubling the extension provided under the Hatch-Waxman Act, and by broadening the scope of claims awarded to allow small firms to control future development. Yet small firms should not be immune from compulsory

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161 *See* Arti K. Rai, *The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, And Access In The Post-Genomics Era*, 2001 U. Ill. L. Rev. 173 (2001) (citing Geneva Pharmaceuticals, Inc. & Abbott Laboratories, Analysis to Aid Public Comment).

162 *See* Christopher Rowland, *Drug Makers Court Small Firms in Push to Fill Thinning Pipelines*, Boston Globe D1 (Mar. 29, 2005); *see also* Ann Grimes & Scott Hensley, *Pfizer Nears a Deal to Acquire Angiosyn, Pad Eye-Drug Roster*, Wall St. J C1 (Jan. 20, 2005).

163 Lansbury, *supra* n. 1, at S54 (proposing a radical mechanism for reducing drug development costs – elimination of Phase III clinical trials by replacement with a limited commercialization mechanism.) While this mechanism may solve the problems of bringing drugs to the market, one can only speculate to the magnitude of liability attached to the limited commercial use of unproven medications. The potential liability alone may prevent new drug entries from reaching the market.

164 *See* John R. Allison, *supra* n. 96, at 42-43 ("The first possible interpretation . . . is that small rather than large entities are the real wellsprings of innovation in the United States. . . . If this interpretation is correct patent law arguably should be doing more than it is to facilitate patenting by small inventors.").

licensing when the use of the patent is deemed abusive or results in gross technology suppression.[165]

Finally, small firms developing orphan drugs have an SV of +2, making it the riskiest scenario in the risk assessment chart. The risk of +2 implies severely insufficient compensation by the current level of patent rewards. Even with the help of government grants, expected returns are often so low that drug development in these cases will not be economically feasible without additional patent support. In addition to increasing the patent term as provided by the Orphan Drug Act and broadening the scope of claims awarded, freedom from compulsory licensing may also be granted.

In cases of collaborative research and development agreements (CRADA), one party usually owns all the intellectual property rights while the others receive rights through licensing. Agreements for joint ownership are uncommon.[166] In this uncommon case, this article suggests that both parties are rewarded according to the party bearing the lowest SV.

B. Transfers of Patent Rights

This article proposes reward adjustments in cases of patent transfers between different entities in the pharmaceutical industry. Non-profit institutions engage in the pioneering research and produce inventions coveted by commercial entities.[167] Revenues from transfers by non-profit institutions, however, often do not fully compensate the investment risks to the investors and the adjustment to patent rewards may be warranted. When the patent rights are transferred to small firms, it may be advantageous to increase the rewards by one in the SV addition chart to the level usually granted to large entities. This increase in support helps account for the high risks still associated with new drugs when they have been transferred at an early stage in development. Small firms developing products using predominantly public funds, however, take on lower risk and should not qualify for a reward increase.

Generally, patent transfers from non-profit organizations to large firms should not qualify for increased rewards. Such an increase might encourage the

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165 *See* David P Hamilton, *Silent Treatment:_How Genentech, Novartis Stifled A Promising Drug: Biotech Firm Tried to Pursue Peanut-Allergy Injection, But Contract Got in Way*, Wall St. J. A1 (Apr. 5, 2005) (describing one example where compulsory licensing would be advantageous).

166 Joint ownership is undesirable where each party can assign, license or sell rights, thereby unilaterally destroying market position of the other party.

167 *See University Start-Up patent Licensing Tactics: Biotech Round Table Discussion*, 42(21) Genetic Engr. News 20 (Dec. 2004).

divestment of risks to the public by large firms that have sufficient funds to carry out research and development.[168] Certain practices, however, utilized in agreements outsourcing research to universities, such as retaining the right to be the first to take an exclusive license to the invention,[169] may justify exceptions to the general transfer rule. For example, a company may provide a university with an unrestricted grant to conduct research in exchange for the rights of first refusal – the rights to patent any inventions resulting from the research.[170] In this case, the investment risks and expectations are still shared by the shareholders of the outsourcing company. Increasing patent support to the level accorded to large firms (as opposed to non-profit institutions) on the SV chart may encourage investment into fundamental research.

While it is desirable to encourage small firms to aggressively invest into the development of new drugs, it is also desirable to facilitate patent transfers from firms that are unable to bring a drug to market to firms that have sufficient resources. To facilitate such transfers, large firms acquiring rights through corporate acquisitions or licensing from small firms may be treated as acquiring all the risks of the small firm; in sales between commercial entities, all the associated risks are usually transferred through the purchase price or royalty agreement. Thus, patent rewards in such cases should be increased to the level accorded to small firms.

In contrast, large firms rarely transfer valuable rights. In such cases, however, the patent rewards may be increased by one increment on the SV chart to account for the risks associated with the future development of these projects.

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168 No more than 20% of inventions developed in some universities are licensed to start-up firms. Most are licensed by more established firms. *Id.*

169 *See* Risa L. Lieberwitz, *The Marketing Of Higher Education: The Price Of The University's Soul*, 89 Cornell L. Rev. 763, 788 (2004) (noting "the 1982 Washington University-Monsanto agreement for $23.5 million of corporate funding over five years in exchange for exclusive licensing rights to patents resulting from the biomedical research; the 1994 MIT-Amgen agreement for $30 million of corporate funding over ten years in exchange for joint rights between the parties to the resulting patents; the 1997 MIT-Merck agreement for $15 million of corporate funding over five years in exchange for licensing rights to resulting patents; and the 1998 UC Berkeley-Novartis agreement for $25 million of corporate funding over five years to the Department of Plant and Microbial Biology in exchange for exclusive licensing rights to approximately one-third of the Department's discoveries.") (footnotes omitted).

170 *Id.*

IV. CONCLUSION

Current patent and regulatory laws are insensitive to economic considerations such as investment risks. These indiscriminant patent rewards tend to motivate the pharmaceutical industry to invest into lower-risk, higher yield projects such as copycat drugs. By taking the investment risks into account, both for the type of pharmaceutical entity as well as the type of drug being developed, this article proposes adjustments to the current level of patent rewards. These adjustments are intended to help motivate the industry towards the development of novel drugs, especially for less common diseases that otherwise would have no treatments available. The general effects, however, of such adjustments on consumers would still need to be evaluated,[171] while the implementation of this proposal requires further study due to U.S. obligations under international treaties.[172]

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171 *See* Adrienne Lewis, *Cipro Saga Exposes How Drugmakers Protect*, USA Today 14A (Oct. 29, 2001), *but see* Alan F. Holmer, *Patent Protection is Key*, USA Today 14A (Oct. 29, 2001).

172 *See* Intl. Leg. Materials, vol. 33(1), 33 I.L.M. 81, 93-97 (1994).