I. INTRODUCTION

A. Overview

> "Over the past two decades, the pharmaceutical industry 'has moved very far from its original high purpose of discovering and producing useful new drugs. Now primarily a marketing machine to sell drugs of dubious benefit, this industry uses its wealth and power to co-opt every institution that might stand in its way, […]."[1]

This is the much-quoted statement of Dr. Marica Angell, the former editor-in-chief of the New England Journal of Medicine. It is a sobering reflection on the operational reality that the development of new medications and improvements to those medications play a crucial role in ensuring continued gains in health and longevity. The need for new medicines is never-ending. To spur the investment needed for the continued research and development ("R&D") of new medicines, economic incentives are essential prerequisites. These incentives can also be provided by intellectual property protection -- particularly patents -- government funding, or other administrative policies. However, achievements of R&D are not enough to provide a constant and efficient flow of new medicines to the market. The pressure exercised by competitors such as generic companies leads to a reduction in drug prices and this too is necessary.

The following purposes of the patent system have been discussed: i) Providing motivations for making useful inventions,[2] ii) disclosing and disseminating information and inventions to the public,[3] and iii) allowing for more efficient exploration of the possibilities inherent in prospective inven-

---

1 *Angell*, 2004, xvii-xviii.

2 *Luski/Wettstein*, 1 Probl. Perspect. Manage. 31, 31 (2004); *Ann*, 2009, 361; *Crouch*, 16 Geo. Mason L. Rev. 141, 141 (2008); *Graham v. John Deere Co*., 383 U.S. 1, 9 (1966) ("The patent monopoly was not designed to secure to the inventor his natural right in his discoveries. Rather, it was a reward, an inducement, to bring forth new knowledge."); *Crouch*, 39 Seton Hall L. Rev. 1125, 1134 (2009); *cf. Kamien/Schwartz*, 1982, 190-91 (noting "[t]he monopolist […] chooses to spend less on development than would a social planner because his reward from innovation is smaller than the total social benefit.").

3 *Friebel et al.,* 2006, 21; *Eisenberg*, 56 U. Chi. L. Rev. 1017, 1028-30 (1989).

tions.[4] The patent system can be used as a way of creating prior art and preventing others from obtaining a patent that an original inventor might later infringe.[5] More importantly, the patent system encourages investment in potentially risky commercialization activities[6] and turns inventions into new goods and services[7] by providing the opportunity to recoup that investment.[8] In other words, it creates the incentives to develop nascent inventions into marketable products, since the prospect of a patent provides greater efficiency in the development of inventions.[9] Jerome Frank J noted in 1942:

> "The controversy between the defenders and assailants of our patent system may be about a false issue – the stimulus to invention. The real issue may be the stimulus to investment."[10]

This function of the patent system can be clearly seen in the responses to the Court of Justice of the European Union ("CJEU") decision,[11] in which the

4 *Kitch*, 20 J. Law Econ. 265 (1977); *Mazzoleni/Nelson*, 27 Res. Policy, 273, 275-80 (1998); *Pfaff v. Wells Electronics, Inc*., 525 U.S. 55, 63 (1998), *reh'g denied* (acknowledging two purposes of the patent system, i.e. "creating and the publicly disclosing new inventions.").

5 *Jaffe*, 29 Res. Policy 531, 539-40 (2000); *Levin et al.*, 1987 Brookings Paper on Econ. Activity, 783, 798 fn. 29 (1987). However, if this was the purpose, it will be the cheaper and easier way to publish the invention to the proper media. *See e.g. Lichtman/Baker/Kraus*, 53 Vand. L. Rev. 2175, 2175-76 (2000).

6 *Roin*, 87 Tex. L. Rev. 503, 509 (2009); *Merges*, 7 High Tech. L. J. 1, 69-70 (1992) ("[P]atents may spur development more than invention per se. […] this may in fact be such an important function that it more than outweighs the contribution patents make to incentives to invent."); *Jaffe/Lerner*, 2004, 43 ("Patents protect an individual's or firm's investment in the development of an idea, as much as they protect the invention itself."); *Svatos*, 13 Soc. Philos. Policy 113, 114 (1996); *Scherer*, 1984, 22-25 (with the example that an investor entered into partnership with the inventor of the steam engine owing to the patent); *Duffy*, 71 U. Chi. L. Rev. 439, 440 (2004).

7 *Kieff*, 85 Minn. L. Rev. 697, 707-12 (2001); *Merges*, 7 High Tech. L. J. 1 (1992).

8 *See e.g., Eisenberg*, 56 U. Chi. L. Rev. 1017, 1036-46 (1989); *Blair/Cotter*, 10 Tex. Intell. Prop. L. J. 1, 78-80 (2001); *Hoffman*, 89 Cornell L. Rev. 993, 1022 (2004) (noting a patent gives an opportunity to recoup R&D costs, thereby providing incentives to invest in further research); *Svatos*, 13 Soc. Philos. Policy 113, 119 (1996) (noting "[j]ust as there is no guarantee that patents will not allow "monopoly" profits, there is also no guarantee that a patent will help capture even normal profits, even if the invention socially useful; this can result from a lack of marketing know-how, excessive litigation costs, etc.").

9 *Kitch*, 20 J. Law Econ. 265, 276 (1977).

10 *Picard v. United Aircraft Corp*., 128 F.2d 632, 643 (2nd Cir. 1942).

11 C-34/10, *Oliver Brüstle v. Greenpeace e.V.*, 2011.

Court held that human embryonic stem cells were not patentable subject matter in Europe. Among the many concerns and objections voiced regarding the decision, the major worries were the impediments to competition in the international market for new disease therapies,[12] and the lack of incentive for innovative companies to invest in this field of R&D in Europe.[13]

The Board of Appeal of the European Patent Office ("BOA") noted in one case that it must be assumed that inventors invent not out of idle curiosity, but with some concrete technical reason in mind.[14] However, it is often observed that inventions may arise as a result of felicitous curiosity, by serendipity, as a result of a flash of insight, or simply due to human nature without recourse to specific grounds.[15] It follows that inventions may arise without patent protection. However, the necessary investment needed to develop such innovation is unlikely to follow without patent protection. With strong protection, companies will invest hundreds of millions of dollars in their R&D in anticipation of substantial reward.[16] Thus, although the patent system is subject to criticism with regard to the high prices that may be entailed by patent protection, there is little doubt that it is crucial to spurring pharmaceutical innovation.[17]

Specifically, the pharmaceutical industry may be regarded as one of those industries in which the economic rationale for patents works best to protect inventors from imitators, provides the incentive for bearing the cost of innovation,[18] as well as ensuring essential protection.[19] However, in spite of this protection, the number of innovative new medicines per year has decreased or remained the same.[20] This seem to undermine the above arguments[21] that patent protection provides incentives for real innovation and promotes the progress of technological development in this field. In addition,

---

12 *Abbott*, 471 Nature 280 (2011) (citing Dr. Brüstle's own word, namely "if we are not allowed to protect our inventions in Germany, we won't be able to compete in the international market for new disease therapies.").
13 *Smith*, 472 Nature 418 (2011).
14 *Agrevo/Triazoles*, T 939/92, OJ EPO 1996, 309, 320.
15 *Crouch*, 39 Seton Hall L. Rev. 1125, 1134 (2009); *Burk/Lemley*, 89 Va. L. Rev. 1575, 1581 (2003).
16 *Scherer*, 20 Health Affair. 216, 220 (2001).
17 *Cohen/Nelson/Walsh*, 2000, 3.
18 *Bessen/Maskin*, 40 RAND J. Econ. 611 (2009).
19 *Roin*, 87 Tex. L. Rev. 503, 513-15 (2009); *Bessen/Meurer,* 2008, 88-89.
20 See subsection III.B.2.
21 See subsection III.A.3.b).

the pharmaceutical industry is facing numerous challenges, such as major capital losses in revenue as the patent terms on some blockbuster drugs have expired, spiralling costs for the development of new drugs, particularly in running clinical trials, more stringent regulatory requirements, and increasingly cost-constrained healthcare systems.[22]

Consequently, the focus has shifted towards alternative strategies of revenue generation. Such strategies may include a move away from creating innovative new medicines in favour of lower-risk solutions, such as improvements or applications. These second generation inventions are also referred to as blocking patents, incremental improvement patents, surrounding patents, fencing patents, and second-tier patents. The strategies used to develop these second generation inventions are referred to as life cycle management, evergreening patenting, patent thicketing, and patent clustering. This increase in the number of second generation inventions in the pharmaceutical industry is particularly worrisome in light of the concomitant dearth of innovative medications and it is questionable whether the movement toward second generation inventions and products is well aligned with the health needs of societies.[23] In addition, second generation patents may adversely impact competition by preventing generic companies from entering into the market or at least making them hesitant to do so.

Since superior new medications are essential to maintaining and improving the health of a society, these concerns about the dearth of new medications and the increase in the number of second generation patents are important and serious. This dissertation will analyze and review whether these concerns are justified, and, if so, whether or how patent law could help to eliminate or lessen these concerns. Amongst others, the following issues will be addressed: Whether the patent system is associated with the dearth of new medications, whether the patent system sufficiently encourages manufacturers to invest in new medications, whether there is a correlation between the increased number of second generation patents and any change in patent law, whether there has been any change in the patentability requirements of second generation inventions, whether all kinds of second generation inventions retain the same value, whether second generation inventions hinder true innovation, such as new medicines, whether second generation inventions delay or prevent the entry of generic products, and, if so, whether and

22 *See e.g., Federsel*, 18 Bioorgan. Med. Chem. 5775, 5775 (2010); *Paul*, *et al.*, 9 Nat. Rev. Drug Discov. 203, 203 (2010).

23 *Avorn*, 309 Science 669, 669 (2005).

how the patent system can improve the situation that confronts pharmaceutical companies and society in general.

B. Outline of the dissertation

This dissertation approaches and analyzes the above issues from various perspectives, mainly within the patent system, and is structured as follows:

Chapter 1 presents a short introduction to the dissertation. Chapter 2 defines the nature of inventions, considers the definition of inventions and innovations in the pharmaceutical art, discusses the range of products in the pharmaceutical market, and explores second generation inventions in pharmaceutical technology along with their backgrounds. Chapter 3 examines the specificities of pharmaceutical development procedure and of the drug markets as well as the central role of the patent system in the industry. It further presents recent challenges, such as the dearth of new medications and efforts to overcome this problem. Chapter 4 revisits the patentability requirements of selection inventions, reviews recent court cases and amended patent examination guidelines and explores the changes therein. Based on the findings in chapter 4, chapter 5 examines concerns about the changes in patentability requirements and assesses the implications thereof with consideration of the scope and the duration of patent protection conferred by second generation patents. Further, an understanding of the implications for competition in the market of generic versions engendered by second generation patents is sought. After reviewing different natures of selection inventions, chapter 6 seeks to formulate proposals on the scope, terms, and patentability requirements of species selection inventions and other selection inventions, to remove uncertainties for private players and users of the patent system and to provide greater benefits to society. Finally, chapter 7 provides a summary and a conclusion.

C. Scope of the dissertation

In the discussion of second generation inventions, the focus will mainly be on chemical selection inventions, such as species selection inventions, optical isomers, metabolites, and crystalline forms. These inventions are chosen not only because they are characteristic examples of second generation inventions, but also because species selection invention can represent fea-

tures of a basic invention. Therefore, they provide a good basis for further discussion of pharmaceutical inventions and innovations. Subsequently, this research results reported in this dissertation could be applied to all other second generation inventions insofar as they also originate from basic inventions.

Jurisdictions are selected based upon an evaluation of the extent of patenting activity and of the pharmaceutical market. Firstly, patenting activity is considered. According to the World Intellectual Property Organization ("WIPO") report,[24] the top five countries for originating Patent Cooperation Treaty ("PCT") filings in 2011 were the United States, Japan, Germany, China, and the Republic of Korea. The combined shares of these five countries accounted for 73.1% of total PCT filings.[25] Furthermore, the top five countries for originating PCT applications in the field of pharmaceuticals in 2011 were the United States, Japan, Germany, France and the Republic of Korea.[26]

The market for pharmaceuticals is further considered, and the number of national phase entries per relevant patent office is analyzed as an indicator of the commercial attractiveness of the country or region. The top five patent offices showing the highest number of national phase entries in 2011 were the offices of the United States, Europe, China, Japan and Republic of Korea.[27] In addition, the actual size of market is considered. According to one report on the pharmaceutical industry, the North American market was the world's largest with a 41.8% share, followed by Europe, accounting for 26.8%, and Japan for 12%, in 2011.[28] In addition, the most highly developed pharmaceutical markets in 2011 were reported to be the United States, Japan, Germany, France, Italy, Spain, Canada, the United Kingdom and the Republic of Korea.[29]

Thus, based on the patenting activities and the importance of the pharmaceutical markets, Germany, the United Kingdom, the United States, and Korea were selected as representative. In addition, the practice before the European Patent Office ("EPO") will be analyzed.

---

24 *WIPO*, 2012.
25 *WIPO*, 2012, 26-27.
26 *WIPO*, 2012, 44.
27 *WIPO*, 2012, 55.
28 *European Federation of Pharmaceutical Industries and Associations ("EFPIA")*, 2012, 14.
29 *IMAP*, 2012, 16.

This paper takes into account the fact that there are other regimes supporting the progress and development of pharmaceutical innovation and securing sustainable access to medicines for the public. Examples would be regulatory exclusivities in pharmaceutical law, prizes, or government funding for research in this area. Nevertheless, this paper will focus exclusively on the patent system. Furthermore, while issues in the area of competition law are not treated exhaustively, such issues will be discussed to the extent that second generation inventions are involved.