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Second Medical Use Patenting: A Review of Practices Across Different Jurisdictions

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Dying new drug pipeline, increasing cost of new drug discovery and generic competition has brought back the focus on drug repurposing. The keen interest in second medical use of known drugs is a sign of trends in the pharmaceutical industry. However, the business potential of the new indication also depends on the availability of patent protection. This study provides a review of the patentability of second medical uses in various jurisdictions. The article reviews different types of claims that are granted by patent offices for second medical uses and the relevant legislations across different jurisdictions.

Keywords: Drug repurposing, patentability, second medical use, Swiss type of claims

Overview of Drug Development

A recent report[1] published by the Tufts Center for the Study of Drug Development (CSDD) pegs the cost of developing a prescription drug that gains market approval at US$ 2.6 billion, a 145% increase, correcting for inflation, over the estimate the Center made in 2003.

The development of new drugs is also extremely time consuming. On an average, it takes about 10-15 years for a new molecule with pharmaceutical efficacy to be developed. This new drug candidate is selected from approximately 5,000 to 10,000 candidates. The rate of success is minimal. After a series of stages of research and development including preclinical research and Phase I, II, and III clinical trials and then finally an approval by the Food & Drug Administration, the drug developer is free to market the drug and reap the benefits of the intense investment. Hence, the innovator tries to garner profits through data exclusivity and patent protection.

In recent years, the pharmaceutical industry has faced several issues[2] delays in the approval process because of the complexity of new products, regulatory changes across the globe, and the changing dynamics of pharmaceutical industry because of mergers and acquisitions and fierce generic competition.

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Protection and Market Erosion by Generics

The innovator protects the drug candidate by various classes of patents. The most important being the product patent which has the broadest sense of protection. After the expiry of the product patent, second and third generation patents namely formulation specific, polymorph or treatment of the approved indication stifle out some generic competition. Even then, after expiry of data exclusivity, the innovator may face competition without patent protection and severe losses due to market erosion.

Business Strategy - A Changing Landscape from Innovation to Repurposing

Cut throat generic competition along with a drying pipeline is changing the landscape of the pharmaceutical industry. Drug repurposing (an approach to drug development that is also known as drug repositioning, reprofiling, or retasking) has become a matter of intense interest during the past few years. As a strategy it calls for reinvestigating drug candidates that have not succeeded in advanced clinical trials, for reasons other than safety, for potential new therapeutic applications.[3]

Some of the companies which have already taken the lead in this interesting arena are establishing themselves as the pioneers in the field including Sosei Group, CombinatoRx, Ore Pharmaceutical Holdings, Biovista; Melior Discovery, Numedicus, Vifor Pharma, Aureus Pharma, Horizon Discovery, Tangent

Reprofiling, Anaxomics Biotech SL, SOM Biotech SL, Switch biotech, Celentyx, and Almac Group.

Thus, the business development model is slowly shifting towards tweaking already approved drugs or drug products. In short, the game has changed from drug discovery and drug development to drug repositioning or drug repurposing. Drug repurposing is one way to extend the life cycle of the product. Changing the formulation, changing the dosage regimen, carrying out clinical studies for a different indication/ disease altogether, developing combinations which show synergy are a few ways for drug repurposing.

Drug repurposing is a scientifically logical process for finding new uses for drugs in well-defined and selected patient populations. Since many agents have already been tested in humans for their safety and efficacy, only the clinical trials with respect to the new indication may have to be carried out. A chance of the failure of the candidate due to toxic side effects is also negligible since the sponsor is already aware of the candidate's clinical performance. Investments are comparatively low and protection can be obtained in the form of patents or data exclusivity. For example, clinical studies for a different indication/ disease can be protected by 'second medical use' patents. They claim new therapeutic uses for known active ingredients. They are an important tool for the innovators who put billions of dollars on research and development of new drugs and come up with ground breaking therapies for the treatment of diseases. Table 1 provides a list of drug candidates that have been tried for repurposing and subsequently launched for the second medical use.

A different types of protections available for the second medical use inventions has been studied. Also, studies have been done on the patentability of second medical use across different jurisdictions which may be of particular importance for the pharmaceutical industry.

Second Medical Use Patents - Protection for Drug Repurposing

Second medical uses may provide solutions to unmet medical needs and significant benefits to patients. They may require significant investment in research and development and represent socially, medically and economically valuable innovations. Basis for second medical use patents can be found in the Article 27 of TRIPS.[5] Article 27 (1) deals with the patentability requirements and state that patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. Articles 27 (2) & 27 (3) deals with exclusions from patentability. Hence, it is still a matter of contention according to TRIPS whether second medical use claims are patentable or not.

Table 1—Representative examples of drugs wherein 2nd medical use not related to first use

Drug name	First use	Subsequent uses
Aspirin	Antipyretic/ Analgesic	Anticoagulant/ Anti-stroke/ Anti-ischemic
Sildenafil citrate	Heart and vascular disease	Treatment of Erectile dysfunction
Nimodipine	Blood pressure	Cerebral disorders
Alfuzosin	CVS	Benign prostatic hyperplasia
Zoledronic acid	Paget's disease	Osteoporosis
Pregabalin	Neuropathic pain	Generalized anxiety disorder
Amphotericin	Antifungal	Leshmaniasis
Bromocriptine	Parkinson's disease	Diabetes Mellitus
Finasteride	Anticancer	Treatment of hair loss
Gemcitabine	Antiviral	Anti-cancer
Methotrexate	Anticancer	Rheumatoid Arthritis treatment
Minoxidil	Antihypertensive	Treatment of hair loss
Raloxifene	Birth control	Osteoporosis treatment
Thalmoid	Morning sickness	Anti-leprosy

Data collated from USFDA approvals on 1 January 2016.

Table 2—Different types of claims for protecting a medical use

Type	Description	Basis
MOT	Claims that clearly recite "a method" (e.g., US-style method claims)	USPTO allows claims to be granted in classic MOT format
Swiss-type	Use of substance X in the manufacture/preparation of a medicament for the treatment of condition Y.	EBA decision G05/83
German-type or Canadian type (Bare use claim)	Use of substance X for the treatment of condition Y	EBA decision G05/83
Purpose-limited product claim format (EPC 2000) (Product-for-use)	Substance X for use in the treatment of condition Y	EPC 2000 came into force in December 2007 EBA decision G2/08

Individual countries have devised their own legal standards with regards to the grant of second medical use claims. For example, European countries allow second medical use claims in a specific format but on the other hand, countries like India, Argentina, and Mexico do not allow second medical use claims to be granted in any form. Second medical use claims are commonly known as method of treatment claims in the US.

Article 27(3) (a) which deals with the exclusions of patentability states that diagnostic, therapeutic and surgical method for the treatment of humans or animals may be excluded from patentability. Countries have interpreted this article as per their own national law. Some members justify denial of patent protection to second medical use claims on the basis that such claims are related to or simply another form of a method of medical treatment, and therefore permissibly excluded from patentability.

- The classic case of second medical use is where a drug is initially developed for a particular therapeutic purpose, and ongoing or later research finds that the drug is useful for another therapeutic area.
- There may also be drugs for which the first known use of the compound did not succeed, but a new use results in an important medicine.
- Sometimes compounds previously discovered for non-medical uses are subsequently found to be effective for medical uses. A related example is the ongoing debate over the potential for various medical uses of marijuana.

Article 27(1) TRIPS states that patents shall be granted to 'any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application'. It is open to question whether TRIPS requires protection for second medical use claims, although some commentators argue that denying patentability to second medical use claims is contrary to TRIPS, particularly Article 27(1).

Traditionally, different countries have used different claim formats for the protection of second medical use. Table 2 provides such claim types namely, method of treatment claims, Swiss type claims, German type claims or purpose limited product claims (EPC-2000 format).

Studies on the relevant legislations for second medical use patents in different countries and the related formats for the second medical use has been carried out. Table 3 provides the relevant legislations for second medical use patents.

Conclusion and Future Perspective

Patenting of second medical use of old molecules is helpful for the drug repurposing. The investment put in for the renewed interest in the old molecules may be covered by the patent monopoly. However, there should be harmonized system for patentability of second medical use as it would assist in the further interest and return on investment for the pharmaceutical companies. The Lack of harmonisation impacts both originator and generic pharmaceutical companies by creating uncertainty for both patent holders and assumed infringers.

Table 3—Relevant legislations for second medical use patents

S No.	Country	2nd Medical use patent	Legislation	Swiss type	EPC 2000	MOT	Bare use type
1	Portugal	Y	EPC Article 53 (C)	No	Yes	No	-
2	Australia	Y	Section 18(2) of Australia's Patents Act, 1990	Yes	No	Yes	Yes
3	Austria	Y	Para 3 Section 3 of Austrian Patent Law, 1970	Yes	Yes	No	-
4	Belgium	Y	EPC Article 53 (3) (c) EPC Article 54 (1) (a) EPC Article 54.4 and 54.5	Yes	Yes	No	-
5	Czech Republic	Y	Novelty, inventiveness and industrial applicability	Yes	Yes	No	Yes
6	Denmark	Y	The Danish Patents Act and the European Patent Convention	Yes	Yes	No	No
7	Canada	Y	The statutory regime is silent on the patentability of second medical uses.	Yes	Yes	No	Yes
8	Finland	y	Section 2 Sub-section 4 of the Finnish Patents Act	Yes	Yes	Yes	Yes
9	France	Y	Article L. 611-11 of the IPC. Article 54 EPC 2000.	Yes	Yes	No	-
10	Germany	Y	EPC Article 52 (1) EPC Article 53 (3) (c) EPC Article 54 (5)	Yes	Yes	No	Yes
11	Greece	Y	Article 5§1b of Law 1733/1987	Yes	Yes	No	Yes
12	Hungary	Y	Act No. XXXIII of 1995 on the Protection of Inventions by Patents (Hungarian Patents Act)	Yes	Yes	No	Yes
13	Ireland	Y	Section 11(4) and (5) of the Patents Act, 1992	Yes	Yes	No	-
14	Italy	Y	Article 46(4) of the Italian Industrial Property Code (IPC)	Yes	Yes	No	Yes
15	Netherlands	Y	Article 54(4) and (5) EPC 2000. Article 4(5) and 4(6) of the Dutch Patent Act	Yes	Yes	No	Yes
16	Sweden	Y	Sections 1d and 2 of the Swedish Patents Act. Section 15	Yes	Yes	No	-
17	New Zealand	Y	Practice note issued on 7 July 1997	Yes	Yes	No	-
18	Spain	Y	Article 6 of the draft of a new Patents Act	Yes	Yes	No	Yes
19	Switzerland	Y	Article 7d Patent Act Article 54(5) EPC	Yes	Yes	No	Yes
20	UK	Y	Section 4A of the UK Patents Act	Yes	Yes	No	-
21	USA	Y	35 U.S.C. § 101 35 U.S.C. § 100(b)	No	No	Yes	No
22	South Africa	Y	Section 25(9) of the Patents Act 57 of 1978. Known substance can only be claimed for use in a method of medical treatment the first time that it isdisclosed as being useful.	Yes	No	No	No
23	Russia	Y	Civil Code Article 1350	Yes	Yes	No	Yes
24	Singapore	Y	Section 14(7) of the Singapore Patents Act	Yes	No	No	Yes
25	Philippines	Y	Republic Act No. 8293, as amended, otherwise known as the Intellectual Property Code of the Philippines.	Yes	Yes	No	-
26	Turkey	Y	NA	Yes	Yes	No	Yes

Contd

Table 3—Relevant legislations for second medical use patents (Contd.)

S No.	Country	2nd Medical use patent	Legislation	Swiss type	EPC 2000	MOT	Bare use type
27	Brazil	Y	BPO's resolution 124/2013 and BPO's guideline	Yes	No	No	No
28	China	Y	Section 4.5.1 Chapter 10 Part II of the Guidelines for Patent Examination (2010 Edition)	Yes	No	No	Yes
29	Bulgaria	Y	Article 6 of Bulgarian Law on Patents and Registration of Utility Models Article 11 (13) of the Regulation on Drafting, Filing and Examination of Patent Applications	Yes	Yes	No	Yes
30	Israel	Y	---	Yes	Yes	No	-
31	Japan	Y	Part VII, Chapter 3 "Medicinal Inventions" The Patent and Utility Model Examination Guidelines	Yes	Yes	No	-
32	Latvia	Y	NA	Yes	Yes	No	Yes
33	Mexico	Y		Yes	Yes	No	No
			Countries which do not provide second medical use patent protection				
34	Venezuela	N	NA	NA	NA	NA	NA
35	Uruguay	N	NA	NA	NA	NA	NA
36	Paraguay	N	NA	NA	NA	NA	NA
37	Peru	N	NA	NA	NA	NA	NA
38	India	N	NA	NA	NA	NA	NA
39	Argentina	N	NA	NA	NA	NA	NA
40	Egypt	N	NA	NA	NA	NA	NA

Data collected from respective patent office website as on 1 January 2016.

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4 Data collated from USFDA approvals on 1 January 2016.

5 Agreement on Trade-Related Aspects of Intellectual Property Rights, https://www.wto.org/english/docs_e/legal_e/27-trips.pdf (accessed on 1 January 2016).

6 Data collected from respective patent office website as on 1 January 2016.