

Exploiting Newly Discovered Indications of Known Therapeutics

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Pharmaceutical companies traditionally spend enormous sums moving a compound from the bench top to the clinic. Each step in the drug discovery process is fraught with risk. Compounds that show enormous promise *in vitro* may lack efficacy or produce unanticipated side effects when moved into the clinic. No wonder that “repurposing” is generating excitement among pharmaceutical companies and academic researchers.

The repurposing approach to drug discovery focuses on the discovery of new uses for known compounds. Because many repurposed drugs are already approved for therapeutic use, the repurposing approach provides an attractive jumpstart that reduces many of the expenses and risks associated with traditional drug discovery.

Perhaps the most striking example of successful repurposing is that of Thalomid (thalidomide). Thalidomide was originally used to prevent morning sickness in pregnant women and later found to cause tragic birth defects. New interest in thalidomide was sparked when scientists discovered that the drug had potent anti-angiogenic and immunomodulatory activities. Thalomid is now approved by the Federal Drug Administration for treatment of leprosy and is the flagship product of Celgene Corporation.

AZT, also known as Zidovudine, is another pharmaceutical that has been successfully repurposed. AZT was originally developed as a treatment for cancer, but was shown to lack efficacy against neoplastic cells. The discovery by Burroughs Wellcome that AZT was effective as a treatment for patients with HIV/AIDS transformed the failed chemotherapeutic into an anti-retroviral blockbuster.

But can the discovery of a new use for an old compound be protected using the U.S. patent system?

Where the new use of an old pharmaceutical product is new, surprising, or unexpected, patent protection generally should be possible. This makes sense from a public policy standpoint. Although the compound itself may be in the public domain, the patent system can reward the inventor who discovers that the compound can be used to treat a new indication. Patent claims directed to the new use will be examined by the U.S. Patent and Trademark Office to see whether the claims define an invention that meets the standards of patentability. To achieve patent protection the invention must be useful, novel, nonobvious, enabled and clearly described in the patent application. For compounds already in clinical use for another indication, novelty may pose a particular challenge.

A new use of the compound that was not explicitly disclosed or appreciated previously may nonetheless face obstacles to receiving patent protection if the new use had been previously “inherently” disclosed. A common inherency situation is illustrated in the following hypothetical example. Let's say that, in March of 2006, a Johns Hopkins University (JHU) researcher discovers that Compound X is useful for the treatment of cancer. The researcher files an Invention Disclosure form with the JHU Office of Technology Transfer that describes the clinical trial where the drug was administered to patients diagnosed with prostate cancer at 1 mg/kg in a timed-release formulation. The Office of Technology Transfer carries out a search of the prior art and identifies a journal article published in January 2004 that reports the results of a Phase III clinical trial where Compound X was administered to a patient four times daily in a 5 mg/kg dosage for the treatment of congestive heart failure. The journal article also mentions that

three of the clinical trial patients treated for congestive heart failure also suffered from lung cancer. The article does not discuss the use of Compound X for the treatment of cancer in any of these patients, and in fact, the prior art failed to recognize any benefit or role of Compound X in cancer. Nevertheless, the U.S. Patent Office would likely allege that the article's disclosure of the administration of Compound X to patients having cancer inherently describes use of Compound X for the treatment of cancer because several of the treated congestive heart failure patients also suffered from lung cancer. This challenge to patentability is not insurmountable, however, if patent claims directed to the new use for cancer treatment are crafted to clearly point out the JHU researcher's new discovery and recognition that Compound X is useful as an anti-cancer agent.

To defeat patent protection for a newly discovered use of a known therapeutic agent, a prior art reference must disclose, either explicitly or inherently, each and every feature recited in a patent claim to the new use of the therapeutic agent. Patentability can be achieved by effectively claiming features that are surprising or unexpected in view of the prior art disclosure. Such features can include a new use of the therapeutic agent for a particular indication or patient sub-population, or use of a particular dosage range or formulation that has not been previously disclosed.

In the above hypothetical, for example, the prior art reference (prior journal article) discloses the administration of Compound X to patients with lung cancer; it does not disclose the administration of Compound X to patients diagnosed with *prostate* cancer. A claim to a method of treating prostate cancer would not be specifically described by the journal article and therefore patent protection for treatment of prostate cancer with the agent may be available. Other claims that may distinguish over the journal article include methods of treating cancer by administering the particular dosage that the JHU researcher discovered was effective (e.g., 1 mg/kg of Compound X) or methods of administering the compound in a timed-release formulation. Other approaches to achieving patentability can include limiting patent coverage to patient sub-populations, such as gender, race or age where an enhanced therapeutic benefit is exhibited within such patient group. Thus, in June 2005, the Food and Drug Administration approved BiDil to treat heart failure limited to a patient population defined by race (this was the first FDA approval limited to a race-defined patient group). The corresponding BiDil patent claims are restricted to use of the therapeutic agent for such a defined patient population.

In choosing to pursue patent protection on inventions directed to new uses of known therapeutics, particularly in academic settings where resources are limited, how likely is there to be a return on the investment?

Academic institutions have enjoyed success in licensing patent applications with claims directed to new uses for known therapeutics. Where a new use is discovered for a compound that is still patent-protected, the company holding the patent is strongly motivated to license the patent application to the new use. Claims to the new use can revitalize a drug whose patent protection is running out. Additional motivation is provided by the company's desire to dominate the market for that drug. They are unlikely to risk that such claims will be licensed to a competitor. Where patent protection to a therapeutic agent has expired, a patent protecting a new use for the drug can generate significant revenues. Generic pharmaceutical companies will be able to sell the drug for indications covered by the expired patent, but will be unlikely to risk charges of infringement for sales relating to the patented new use.