The Fine Art of Patent Weaving

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While consumer advocates sometimes view patents as being the light swords of the evil pharmaceutical empire, those of us with front row views of the massive costs accrued in bringing drugs to market appreciate that without the profit guarantees that patents afford, there would be no motive to fund innovation. More than once I have seen exciting therapies wither on the vine because too much time has passed since a patent application or because a prior art jungle was too thick. Like most of us in this industry, I am largely motivated by the desire to get better treatments to patients, and it saddens me to see potentially life-saving technologies get passed over. However, I can't promise that I would throw my own money, were it not already invested in my wife's exquisite design sense, on an unsure bet knowing that the payoff would be limited to a few years of market exclusivity. If intellectual property protection is evil, it is a necessary evil in ensuring funding of innovation.

Given the importance of intellectual property to our clients, it is not surprising that we at PharmaDirections spend a good deal of time and effort seeking tortuous pathways through prior art and, like collage artists, piecing together bits of technology in unique ways until an image of novelty emerges like the Virgin Mary arising from a grilled cheese sandwich. It is an exercise that requires the knowledge of a scientist, the creativity of an artist, the inquisitiveness of a detective, and at least two semesters of Lawyerese as a second language. As long as your body can tolerate enough caffeine to get through all the "comprises," "embodiments," and "as will be understood by those skilled in the arts," it can actually be quite fun.

There are two aspects of generating IP and both require a well-oiled collaboration between experts in relevant disciplines and a good patent attorney. The first of these aspects is finding openings in the prior art, or as we lovingly refer to it, "patent busting," and the second is building new technology within those openings, or "patent building." Although these sound sequential, they ideally are not and in fact should be interactive. Ideas generated in scouring through patents and literature can be tested experimentally and the results generated can serve as fodder for additional probing of documents.

As an example, I was tasked a few years ago with generating a non-infringing and patentable formulation for a very well-established drug substance that was to be used in a novel combination product. The drug needed to be stabilized to attain shelf life, and about 25 patents had been issued covering every reasonable aspect of how to do this. I assembled two teams, with some overlapping membership. One team, composed of some of PharmaDirections' best creative geniuses, was tasked with reviewing the patents and

other literature while the other, which included more practically minded technologists, was tasked with designing experiments and prototypes. Both teams met weekly, with the crossover members conveying the results of one team's enquiries to the other team so that those results could be factored into the next round of enquiries. Less frequent meetings were held with a patent attorney to validate our thoughts. Several of PharmaDirections' preferred vendors were used in parallel to carry out the experiments. Surprisingly, most of all to us who were entrenched in the thicket with our machetes, we were able to generate a path forward and develop defendable new IP within only a few intense months.

As might be expected, many of our clients hold assets with waning patent lives and need to generate new protection through novel dosage forms. With the patent office taking a stricter view of obviousness in recent years, just generating an extended release formulation is usually not enough. It doesn't take an Einstein or Edison to figure out that QD dosing is better than TID, so examiners tend to accept only very narrow claims around controlled release formulations, making it easy for competitors to "formulate around" the covered dosage.

An approach we have used successfully for several clients is to use complex computer models to identify novel aspects of a drug's pharmacokinetics and pharmacodynamics and then use these novel aspects as the basis for a controlled release formulation. In one case we discovered *in silico* and confirmed clinically that a well-studied drug had a surprisingly narrow window of release rates within which C_{max}-related side effects could be muted without substantial loss of AUC. In another case, we started with receptor occupancy data and used that to generate a PK profile, which we then used to derive an optimal controlled release profile, which then became the target of our formulation efforts. In virtually all cases, we have been able to find some unexpected quirk of the PK itself and/or of the formulation requirements for meeting the optimal PK. As such, we have been able to incorporate aspects of the target PK profile into multi-pronged IP portfolios, affording our clients much broader protection than could be obtained from a formulation alone.

Sometimes someone sneezes in a petri dish and intellectual property just happens, but more often than not it needs to be searched out and developed. Setting out to search for the unexpected sounds like a quest more appropriate for Jack Kerouac than for a pharmaceutical scientist, but in essence this is exactly what we do in trying to generate IP protection. One needs a strong background of knowledge, a penchant for details, a large amount of creativity, an even larger amount of strong coffee, and, most importantly, a very open mind. Enjoy the road.

About PharmaDirections

PharmaDirections is a consulting and project management company with a unique approach to managing preclinical, CMC and regulatory affairs programs. PharmaDirections provides strategic planning then oversees and directs pharmaceutical contract research using our own scientific experts and project managers. We are a comprehensive R&D resource for pharmaceutical and biotech companies who need more than just outsourcing of their API or drug product development.