STRATEGIES FOR CREATING AND PROTECTING DRUG PATENTS

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Patents on 65 drugs with weekly sales in the $2 to $10 million range expired in 2003. Loss of market share is estimated to be about 40% within the first year after patent expiration. In addition, the pharmaceutical pipeline is "drying" up – i.e., fewer new drugs are entering the market. Therefore, when the patent on the drug expires, pharmaceutical companies are increasingly seeking patent extension of the drug through innovative approaches such as clinically superior formulations of the drug (e.g., new drug delivery systems, controlled release) and chemico-pharmacological (i.e., improvements in the pharmacokinetics or side effect profiles, single isomer drugs) modifications. However, a clear understanding of the underlying science, and patent and drug law (i.e., Hatch – Waxman Act) are critical to the success of such attempts at patent extension. The loss of patent extension with three "blockbuster" drugs (*infra*) during 2000-2002 clearly showed a lack of such understanding. A major reason for this lack is that though, creation and protection of drug patents require collaboration between scientists and attorneys ("Scientists Invent, Lawyers Patent"), these two groups do not communicate effectively "[b]ecause there is a general lack of understanding of each culture, [and] these interactions often lead to a cognitive friction that is both disturbing and costly to society" (A Convergence of Science and Law, National Academy Press, 2001). In addition, recent (August 2003) FDA regulations will place efforts to extend patent extension under stricter scrutiny.

The 3 drugs where attempts for patent extension failed were fluoxetine (Prozac®), omeprazole (Prilosec®) and buspirone (Buspar®). These infringement cases between generic and brand name pharmaceutical companies arose after generic companies sought FDA approval of generic versions of brand (patented) drugs under paragraph IV certification of the Hatch-Waxman Act. The patent-extension attempt by Eli Lilly for Prozac® failed because it was found to involve double patenting. Two method patents were involved in the Prozac® patent infringement case of Eli Lilly against generic manufacturers. On appeal, the trial Court decision was reversed and it was held that the claim 7 of the "549" patent was invalid for obviousness-type double patenting in view of claim 1 of the "895" patent. Essentially, both claims were found to be directed towards treating anxiety using fluoxetine. Claim 1 of the "895" patent claimed a "method to block the uptake of serotonin by brain neurons in animals" by administering

fluoxetine. Claim 7 of the "549" patent claimed a **"**method for treating human suffering from depression" by administering fluoexitine. Since the mechanism of action of fluoxetine in the treatment of depression involves blocking neuronal uptake of serotonin, the two claims are the same. Therefore, the probability was high that, in view of the underlying science, a court would find this strategy to be double patenting. It appears that this crucial point was not appreciated by the Eli Lilly team. Development and marketing of innovative formulations prior to the Prozac® patent expiration could have been more successful in extending the patent life of this drug.

Attempts by Astra to extend its formulation patent (i.e., Prilosec®) failed because the company appeared to have ignored the possibility that their patent could be "designed around" using new formulation technologies. The main issue in the Prilosec® infringement case was whether the "core" of the generic microtablet of omeprazole (the alleged infringing product) contained "an alkaline reaction compound (ARC)" also found in the patented (the "505" patent) formulation; since omeprazole is unstable in the acid environment of the stomach, the ARC (basically, a "buffering" agent) serves as protective agent. The Court held that there was no infringement of the Prilosec® patent by the generic microtablet because "[it was]… designed around the '505'… patent by developing a formulation that did not require an ARC in its core". It would appear that a better strategy to extend the patent life of omeprazole would have been to patent different dosage forms of the drug without an ARC or based on different technologies to limit "designing around" opportunities for competitors.

In the Buspar® case, two Bristol-Myers Squibb (BMS) patents were involved: one for the drug (buspirone, the patent "763") and the other for an active metabolite of buspirone (the "365" patent). In the infringement case by the innovator against its generic competitors, the Court rejected the argument of BMS that the metabolite patent covered the use of its parent drug, thus enabling marketing of generic buspirone. Again, an environment, where patent attorneys and lawyers have a very close working relationship would have identified the weakness of this strategy since the drug and its metabolite(s) are different chemical entities. In addition, there is case history that would have served as a warning of the weakness of this strategy. Subsequently, Attorney Generals of 35 states sued BMS for violating antitrust laws (i.e., anticompetitive acts) in connection with Buspar®. On going litigation so far has cost BMS hundreds of millions of dollars in settlement costs.

In conclusion, for more efficient creation of patents and subsequent protection of their intellectual "offspring", pharmaceutical scientists and patent attorneys need to (1) understand the underlying concepts and principles of the other's discipline relating to patents and (2) work closely during the life cycle of the drug to extend its patent life.