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# The Patent Use Code Conundrum – or Why FDA Can't Read (Patents)

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When Hatch-Waxman was adopted 30 years ago, Congress wanted to ensure that generic manufacturers could enter the market with low cost drugs just as soon as the initial protections on the brand drug had expired. Specifically, Congress was concerned about "evergreening," whereby new, protected indications might be added to the brand label to thwart generic entry and extend the life of the drug monopoly. Congress said there was no reason why a generic drug could not be approved for older, unprotected uses at the same time the brand was being sold for newer uses protected by patent or exclusivity.

Thus, Hatch-Waxman allows an ANDA applicant who does not intend to market its drug for a protected use, to "carve out" of its label (which otherwise must be identical to the brand) all information associated with that protected use. As long as the now "skinny labeled" generic was no less safe or effective as the brand for all the remaining uses, it would receive an AB-rating as a therapeutic equivalent (TE) to the brand drug for the labeled uses. The obvious restriction was that the skinny labeled generic could not be marketed or advertised for the protected use carved out of its label and now considered an "off-label" use of the generic drug. Congress left to the FDA the task of determining what language on the brand label was or was not covered by the protected use.

For uses protected by three-year exclusivity (awarded for new uses based on clinical studies), the FDA's carve out analysis is relatively straightforward because it is the sole arbiter of the language to be added to the brand label based on the clinical studies; thus, it knows exactly what language needs to be carved out by a skinny labeled generic. For uses protected by patent, however, the FDA's carve out analysis is much more difficult because it refuses (or, as the FDA contends, is not specifically authorized) to develop any requisite patent expertise. Therefore, to make the patent carve out calculus easier the FDA requires NDA holders to submit for Orange Book listing, a short statement describing the approved use claimed by the patent, known as the patent "use code." The FDA then can rely on the use codes to determine what language a skinny labeled generic must remove from its label in order to be approved. When the patent use code and brand label language are literally the same, the carve out analysis is easy; but when the use code and label language are not identical, which is more often the case with therapeutic use patents, the carve out analysis is much harder because the FDA does not read or construe patent claims. This can lead to a legal conundrum whereby a skinny labeled generic goes to market with an FDA-approved drug label that, in fact, induces infringement of a brand patent listed in the Orange Book. And because courts are loathe to enjoin the sale of low cost generic drugs once on the market, brand drugs protected by use patents are in a potentially precarious position.

## Hospira Case Spotlights Issue

This issue was brought to the fore recently in a case involving Hospira's sedation drug, Precedex. In a nutshell, the drug was approved for two indications: (1) sedation of initially intubated patients in an intensive care setting; and (2) sedation of non-intubated patients prior to and/or during surgical and other procedures. Precedex was also protected by a use patent whose listed use code that had recently been amended by Hospira to read: "intensive care unit sedation including

sedation of non-intubated patients prior to and/or during surgical and other procedures." Several generic manufacturers wanted to carve the use code out of the brand label; however, an ordinary construction of the use code appeared to read on the two approved indications because it claimed both sedation of patients in an ICU as well as the sedation of non-intubated patients (who might also happen to be in an ICU) prior to and/or during surgical or other procedures. Construed in this fashion, the Precedex use code could not be carved out of a generic label because there would be no remaining indication for the drug.

Not sure as to what it should or could do in this case, the FDA requested public comment on its options. In the end, it concluded that "so long as any express reference to the protected use is omitted from the labeling" any possible overlap of the broad use code (ICU patients) and the second indication (non-intubated patients generally) was permissible under Hatch-Waxman. Shockingly, this was an admission that the Hospira patent, as described by its use code would, in fact, be infringed by an FDA-approved generic drug – and moreover, that this was sanctioned by Hatch-Waxman.

The FDA's decision was appealed to the District Court in the Southern District of Maryland which temporarily enjoined the FDA from approving any skinny labeled generics, but after briefing, upheld the carve out decision as a proper exercise of the FDA's authority under the Administrative Procedure Act (APA). See Hospira v. Burwell, No. GJH-14-02662, slip op. (D. Md. Sept. 5, 2014). In its lengthy opinion, the court seemed oblivious to the fact that the APA is not the only governing statute that the FDA is required to follow but that it is also responsible for following Hatch-Waxman's homage to the patent statutes that a generic drug should not be approved under a use carve out if the remaining generic labeling instructs users (any users) to practice the patented method of use. On this issue the relevant case law is clear.

Other Cases Provide Clarity

In AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1060 (Fed. Cir. 2010), the Federal Circuit found a skinny label generic to infringe even though the carved out label did not explicitly describe the claimed use (once a day administration) because, the court reasoned, it instructed a "downward titration" that effectively directed a lowest-beginning-dose user (i.e., one taking the lowest strength twice daily) to titrate down to once daily, since there was no other way for such user to titrate lower. The court said it was not a matter of claim specificity but whether the proposed label language would "inevitably" lead some users to practice the claimed method of use.

In Bone Care Int'l, L.L.C. v. Roxane Labs., Inc., 2012 U.S. Dist. LEXIS 80450, 33, 2012 WL 2126896 (D. Del. June 11, 2012), a generic drug was found to inherently infringe in some patients because the labeling instruction to administer the drug "for the treatment of secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease on dialysis" would induce infringement of a patent claiming the administration of the drug for the treatment of end stage renal disease (ESRD) and SHPT "because patients with chronic kidney disease on dialysis suffer from ESRD and the majority of patients with ESRD also suffer from SHPT."

More recently, in L.A. Biomedical Research Institute at Harbor-UCLA Medical Center v. Eli Lilly and Co., et al. at 6-7 (C.D. Cal. N0 2:13-cv-08567-JAK-JCG, motion dismissed), a label containing the phrase "for the treatment of ED" was found to specifically intend for the drug also to be taken "for the treatment of penile fibrosis" (patent claim language that did not appear on the label) because "symptoms suffered by many ED patients are caused by an underlying penile fibrosis condition [and thus] the label will inevitably lead some consumers to practice the claimed method."

And finally, there is no escaping the holding in Caraco Pharmaceutical Labs. v. Novo Nordisk A/S, 132 S.Ct. 1670 (2012), wherein the Supreme Court found a patent use code to be unlawful because it prevented generic entry for an approved use not claimed by the patent, and then observed, prophetically, that "the FDA will not approve an ANDA if the generic's proposed carve

out label overlaps at all with the brand's use code." Read plainly and holistically (and not as mere dicta that "turns logic on its head" as the district court said in its Hospira decision) this observation would seem to capture the essence of how the patent and drug laws were designed to intersect under Hatch-Waxman.

Thus, we have the patent use code conundrum presented by Precedex: an FDA carve out decision that may be lawful under the APA but nonetheless, sanctions an infringing use expressly prohibited by Hatch-Waxman and the patent statutes. The real problem is that this seems to keep happening as the recent case law shows. This is not likely what the framers of Hatch-Waxman had in mind. More likely, what they had in mind was that the FDA would eventually hire some patent attorneys.