The Fed. Circ. In April: Hurdles Remain For Generics

By **Sean Murray and Jeremiah Helm** (May 3, 2024)

This article is part of a monthly column that highlights an important patent appeal from the previous month. In this installment, we examine the Federal Circuit's recent ruling in Salix Pharmaceuticals v. Norwich Pharmaceuticals, and what it means for selling generic drugs with invalidated patents.

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In the original Pyrrhic victory in the third century B.C., Greek King Pyrrhus of Epirus crossed the Adriatic Sea to southern Italy and fought three battles against the mighty Romans.

Using heavy cavalry and war elephants, Pyrrhus achieved two unlikely victories against a much larger Roman army. But his army also suffered heavy losses and, after fighting a third battle to a stalemate, Pyrrhus was forced to return to Greece with nothing to show for his six years of fighting in Italy.

An April U.S. Court of Appeals for the Federal Circuit decision describes a more modern Pyrrhic victory after a hard-fought campaign in the U.S. District Court for the District of Delaware, the battlefield of choice for pharmaceutical patent litigation.

In Salix Pharmaceuticals Ltd. v. Norwich Pharmaceuticals Inc., the Federal Circuit affirmed in all respects a District of Delaware decision that blocked Norwich's abbreviated new drug application, or ANDA, to sell a generic version of Salix's antibiotic rifaximin.

In a hard-fought case, Norwich succeeded in invalidating Salix's patents on a treatment method using rifaximin.

Ordinarily, this means the generic manufacturer's ANDA will be approved, and its product will be cleared to launch. But in a strange twist, the district court ordered the U.S. Food and Drug Administration not to approve Norwich's ANDA until at least October 2029.

The result was a Pyrrhic victory for Norwich that provides useful lessons for drug manufacturers who wish to market a generic version of a pharmaceutical used to treat multiple medical conditions.

The dispute began when Norwich filed an ANDA seeking approval to sell generic rifaximin for two purposes: treating hepatic encephalopathy, or HE, and treating irritable bowel syndrome with diarrhea, or IBS-D.

In response, Salix filed a patent infringement suit asserting that Norwich's sale of rifaximin to treat HE would infringe three of its method patents, and its sale of rifaximin to treat IBS-D would infringe two other method patents. Salix also argued that selling Norwich's generic drug for either purpose would infringe two patents covering polymorphic forms of rifaximin.

Norwich's primary defense was its claim that Salix's patents were invalid as obvious. But Norwich faced an uphill battle.

To gain the right to sell its polymorphic form of rifaximin to treat HE, Norwich needed to invalidate Salix's three patents on methods of treating HE and its two patents on polymorphic rifaximin.

To sell polymorphic rifaximin to treat IBS-D, Norwich had to invalidate Salix's two patents on methods of treating IBS-D, as well as its two patents on polymorphic rifaximin. This was no easy task given the presumption of validity accorded issued patents and the concomitant requirement that obviousness be proved by clear and convincing evidence.

Against all odds, Norwich succeeded in invalidating all four of the patents blocking it from selling polymorphic rifaximin for IBS-D.

In a pair of victories reminiscent of Pyrrhus's first two battles against the Romans, Norwich invalidated both the IBS-D patents and the polymorphic rifaximin patents.

With respect to the IBS-D patents, the district court found the patents obvious in view of a 2006 journal article and a clinical trial protocol that had been published on the ClinicalTrials.gov website in 2005. Salix did not dispute that these references disclosed the limitations of the asserted claim or that a person of ordinary skill in the field would have been motivated to combine the references.

Instead, it argued that a person of ordinary skill would not have had a reasonable expectation of success in combining the references to obtain the claimed inventions. The district court disagreed.

With regard to the polymorphic rifaximin patents, the district court found the claims obvious over a prior art patent and the common knowledge of a person of ordinary skill in the field. Salix argued that a skilled artisan would have lacked a reasonable expectation of success in producing the specific polymorphic form of rifaximin recited by the claims, rifaximin beta.

However, the district court found that the prior art patent disclosed several preparation protocols for rifaximin that would have produced rifaximin beta, and that a routine characterization of the rifaximin resulting from those preparation protocols would have detected its presence. A skilled artisan would have had a reasonable expectation of success because such characterization was routine and could have been performed in a single day.

The Federal Circuit affirmed all of these findings.

After its twin victories invalidating Salix's IBS-D patents and its polymorphic rifaximin patents, Norwich might have reasonably expected to be permitted to sell generic rifaximin beta for the treatment of IBS-D. But this is where things changed for Norwich.

The district court ruled that Norwich infringed Salix's method patents for treating HE and that these patents were valid. It then ordered the FDA to defer any approval of Norwich's ANDA until the HE patents expire in October 2029.

Norwich argued that its ANDA could be approved immediately for the noninfringing IBS-D indication. To no avail. The district court relied on Title 35 of the U.S. Code, Section 271(e)(4)(A), which provides that, where a district court finds an "act of infringement," any "approval of the drug ... involved in the infringement" shall be deferred until after the expiration of the infringed patents.

Norwich pointed out that its sale of generic rifaximin beta for treatment of IBS-D would not infringe any valid Salix patent. The district court ruled, however, that the act of infringement was the filing of an ANDA reciting an infringing use, namely, treating HE with rifaximin.

Norwich amended the language in its ANDA to eliminate references to treating HE with rifaximin. Norwich then sought relief from the judgment under Rule 60(b) of the Federal Rules of Civil Procedure. But the district court declined to exercise its discretion modify the judgment.

According to the court, it was unclear whether the amended language would still induce physicians to use Norwich's drug to treat patients with HE, and resolving this infringement issue would essentially require a second litigation.

This is how Norwich's twin successes in invalidating Salix's IBS-D and polymorphic rifaximin patents were transformed into Pyrrhic victories, at least for the moment. One suspects this saga is not over.

The Salix decision provides useful lessons for patent practitioners. For example, when the seller of a brand-name drug has separate method patents protecting each indication, an ANDA filer should consider whether it makes sense to list each indication in its ANDA.

If one indication is protected by patents that are more likely valid and infringed than the patents protecting the other indications, omitting that best-protected indication from the ANDA may be the better part of valor.

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