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Federal Circuit Affirms Invalidity and Non-Infringement of Patent for Compound Used to Ameliorate Effects of Cancer Treatment

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On October 2, 2015, the Federal Circuit affirmed a district court's holding (1) that a *substantially* pure compound would have been obvious when a lesser pure compound ("the 50/50 mixture") and the pure compound were known in the art; and (2) that applicants' actions during prosecution of the patent-in-suit precluded the use of the doctrine of equivalents to prove infringement. *See Spectrum Pharms., Inc. et al. v. Sandoz Inc.*, No. 15-1407, slip op. (Fed. Cir. Oct. 2, 2015).

Substantially Pure Compound Was Held Obvious Over Both a Mixture and a Pure Compound

In *Spectrum*, the court was faced with an unusual obviousness question: "whether a *substantially pure* compound would have been obvious when both the 50/50 mixture and the pure compound were known in the art." *Id.* at 11. Here, the compound at issue was leucovorin, which may exist as a 50/50 mixture of two diastereoisomers—the (6S) and (6R) isomers. The (6S) isomer exhibits desired biological activities.

The court reasoned that "[i]f it is known that the desired activity all lies in one isomer, surely, it is better, and there is generally motivation, to try to obtain the purest compound possible. . . . A physician would not likely want to administer a contaminant or a less pure material to a patient if one could use a pure material. Thus, there is always in such cases a motivation to aim for obtaining a pure, resolved material." *Id.*

Indeed, the court found that the knowledge of the desired activity stemming from the (6S) isomer provided the requisite motivation even without an explicit teaching. *Id.* at 12. Thus, "there was no need to find an express teaching to prove sufficient motivation to modify the prior art to arrive at the claimed invention, where various techniques to purify the isomers were reported in the art and, importantly, it was known that the (6S) isomer alone provided the therapeutic effect." *Id.*

While the motivation to purify the 50/50 mixture was clear, the court noted that if one were to start with the known pure compound, there is "no reason . . . why one would want to have an impure material." *Id.* at 11. Nevertheless, the court found that the "less-than-pure material" did not show any unexpected advantages over the prior art pure material such that the claimed substantially pure compound was not nonobvious. *Id.* at 12. Spectrum's expert confirmed the obviousness, testifying that the claimed substantially pure compound "offers no meaningful difference" from the pure compound. *Id.* at 14.

Applicants Statements to the USPTO Disclaimed Lower Dosage Quantities

The Federal Circuit further affirmed the district court's decision on summary judgment that Sandoz's ANDA product did not infringe 5-9 of the '829 patent because Spectrum had not shown literal infringement and was estopped from applying doctrine of equivalents. The central issue of non-infringement centered around the dose quantity.

Specifically, the *Spectrum* court held that Sandoz's ANDA product would not infringe the asserted claims because Sandoz's product would be sold in single-use vials with 175 mg or 250 mg of substantially pure levoleucovorin (*i.e.*, the (6S) isomer) and dosed between 7.5 mg and 75 mg per dose. *Id.* at 17. In contrast, the claims required at least two doses of 2000 mg each. *Id.*

Furthermore, during prosecution, in response to an office action, the patentees expressly limited the dose quantity by adding new claims (which eventually issued as claims 5-9) that "include specific limitations as to quantities of materials," and "quantity limitations set forth in the claims" which "define an aspect of the invention that is of great practical significance." *Id.* at 17. Indeed, the applicants further argued that a prior art reference did not teach the claimed compositions "in the quantity specified" in the newly added claims. *Id.* at 18. Accordingly, the court concluded that "[t]hose statements are clear and unmistakable expressions of the applicants' intent to surrender coverage of quantities of the compound in lower doses" such that prosecution history estoppel barred Spectrum from invoking the doctrine of equivalents. *Id.*

For patent litigants, the *Spectrum* decision provides guidance for attacking the validity of claims directed to the purity of a compound within a pharmaceutical composition, and finding motivation to modify the prior art based on conventional knowledge in the field as opposed to an explicit teaching. This decision also reaffirms the importance of detailed analysis of any asserted patent's prosecution history to identify disclaimers that allow for a possible design-around, both literally and under the doctrine of equivalents. For patent prosecutors, the *Spectrum* decision highlights the importance of carefully considering amendments to the claims that could in the future be used to prevent application of the doctrine of equivalents.

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