Dissent Exposes Flaws In Fed. Circ. ANDA Patent Holding

By **Daniel Pereira** (September 16, 2019)

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Nalpropion Pharmaceuticals Inc. v Actavis Laboratories FL Inc.[1] is a precedential U.S. Court of Appeals for the Federal Circuit opinion written by U.S. Circuit Judge Alan Lourie with U.S. Circuit Judge Evan Wallach and a dissent from U.S. Circuit Judge Sharon Prost in a case that arose from the filing of an abbreviated new drug application litigation in which Actavis sought approval for its generic version of Nalpropion's Contrave product. Footnote 1 in the opinion outlines the rather complex history of the ownership/license interests as they changed over time.

The opinion address questions of written description and obviousness of certain claims of the patents-in-suit. For present purposes, I found the dispute between the majority and the dissent centered on claim 11 of U.S. Patent No. 8,916,195 to be the most interesting as it addresses the questions of claim interpretation and the written description requirement. That claim is:

A method of treating overweight or obesity having reduced adverse effects comprising orally administering daily about 32 mg of naltrexone and about 360 mg of bupropion, or pharmaceutically acceptable salts thereof, to a person in need thereof, wherein the bupropion or pharmaceutically acceptable salt thereof is administered as a sustained release formulation, wherein the naltrexone or pharmaceutically acceptable salt thereof is administered as a sustained release formulation, and wherein said sustained release formulation of naltrexone has an in vitro naltrexone dissolution profile in a dissolution test of USP Apparatus 2 Paddle Method at 100 rpm in a dissolution medium of water at 37° C. of:

a) between 39% and 70% of naltrexone released in one hour;

b) between 62% and 90% of naltrexone released in two hours; and

c) at least 99% in 8 hours;

wherein about 16 mg of said sustained release formulation of naltrexone or a pharmaceutically acceptable salt thereof is administered twice daily, and about 180 mg of said sustained release formulation of bupropion or a pharmaceutically acceptable salt thereof is administered twice daily.

The center of the written description dispute is the in vitro dissolution profile.

Actavis argued that claim 11 of the '195 patent lacked adequate written description support because its claimed dissolution profile was achieved using the United States Pharmacopeia Apparatus 2 Paddle Method, but the specification discloses data obtained using the different USP Apparatus 1 Basket Method. The court was not persuaded that the use of a different method from what is prescribed in the claim presented a written description problem, holding that "whether the dissolution data reported in the specification was obtained using the basket method or the paddle method is not relevant to whether the inventors had possession of the invention."

The majority and the dissent disagreed as to what import to provide the dissolution profile. Judge Lourie, writing for the majority, opined that the "dissolution profile for naltrexone as

measured by USP 2 relates only to the measurement of resultant in vitro parameters, not to the operative steps to treat overweight or obesity."

Therefore, the trial court and the Judge Lourie found that the method of treatment requirement was orally administering a sustained release dosage of two actives, naltrexone and bupropion, in required amounts. The dissolution profile does not change the nature of this method of administering but simply defined the parameters of the sustained release of the actives to the patient ("resultant dissolution parameters rather than operative claim steps."). This conclusion, coupled with expert testimony as to the substantial equivalence between the two methods of assessing sustained release, was supported by the required factual findings from the lower court.

Judge Prost did not agree:

I part ways with the majority, however, for at least three reasons. First, the USP 2 clause is limiting. Second, the majority's "substantially equivalent" rule is inconsistent with this court's precedent. Third, the district court clearly erred in finding that the '195 patent's written description includes a disclosure "substantially equivalent" to USP 2.

Judge Prost viewed the dissolution profile as defining a key characteristic of the formulation that is administered. As noted by Judge Prost: "The amount of sustained-release carrier determines the in vitro release rate (dissolution) profile of the naltrexone formulation. ... Thus, the dissolution profile, as measured using USP 2, reflects the amount of sustained-release carrier included in the orally administered naltrexone formulation."

This is key and indeed was a point made during prosecution in the U.S. Patent and Trademark Office — as noted by Judge Prost: "Applicant argued that, having used a different method, there was no basis to conclude that the prior art inherently disclosed a formulation that falls within the claimed dissolution profile."

The dissent seems like a better conclusion and more consistent with years of jurisprudence on description/possession. The formulation of drug dosage forms can significantly alter the release profiles of the drug(s) contained in the formulation, from rapid and immediate, delayed over the course of 24 hours, and release in certain portion of the gastrointestinal tract, e.g., stomach or duodenum. Here the patentees defined the formulation not in terms of what components were in the formulation, the relative amounts of the components and/or how the components are mixed together to yield a resultant release profile.

For instance, in 1928, the U.S. Supreme Court held that it is not proper in a patent to claim a product solely in terms of its novel properties. In Holland Furniture Co. v. Perkins Glue Co.,[2] the patent in suit claimed: "A glue comprising cassava carbohydrate rendered semifluid by digestion [i.e., a starch glue] and having substantially the properties of animal glue" That is, the claim covered a starch glue having the properties of an animal glue, and held such claims to be invalid for being overly broad:

But an inventor may not describe a particular starch glue which will perform the function of an animal glue and then claim all starch glues which have those functions.

A claim so broad, if allowed, would operate to enable the inventor, who has discovered that a defined type of starch answers the required purpose, to exclude others from all other types of starch, and so foreclose efforts to discover other and better types. The patent monopoly would thus be extended beyond the discovery, and would discourage rather than promote invention. The attempt to broaden product claims by describing the product

exclusively in terms of its use or function is subject to the same vice as is the attempt to describe a patented device or machine in terms of its function.

Similarly, in General Electric Co. v. Wabash Appliance Corp.,[3] the Supreme Court invalidated claims that recited no novel structure, but rather used "conveniently functional language at the exact point of novelty." Judge Prost relied on more recent jurisprudence in his conclusions. but at the end of the day, the dissent's view is more consistent with the question of possession of an invention.

The issue of written description is one of fact, and such questions of fact are reviewed for clear error. How the majority reviewed that question and to what it give most importance is the highlight of this case. The majority gave more weight and credence to the expert testimony, as did the district court ("[t]he district court performed precisely its fact-finding function, weighing credibility of testimony.").

Yet, as Judge Prost noted in his dissent, there was no evidence to support the notion that the two manners of determining the dissolution profile were substantially equivalent, and, rather, there was evidence that they were not equivalent. Yet the majority opinion and the trial court choose to ignore and/or discount that contrary evidence.

Had the majority focused on the question of whether possession of one dissolution test was sufficient for another dissolution test the majority opinion would be far less confusing. This would not diminish the dissent's position that there were insufficient facts, and rather contrary facts, that did not support the substantial equivalence of the two dissolution tests.

Nonetheless, the holding that a "wherein" clause that defines specific parameters of a formulation that is administered to a patient is nonlimting is likely to open upon some unintended doors in the prosecution of patent applications and inter partes patent disputes.

If the clause in question is nonlimiting, can it be used to properly distinguish over prior art (as was apparently done during prosecution)? Can an applicant include a claim limitation that is not supported, ipsis verbis, in the disclosure but present evidence that the limitation is a substantial equivalent to what is disclosed in the application? In any event, the new rule as stated by Judge Prost is: "written description for nonlimiting clauses may be satisfied by disclosure that is 'substantially equivalent' even though the same disclosure would not be sufficient for limiting clauses."

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[1] Nalpropion Pharmaceuticals, Inc. v Actavis Laboratories FL, Inc. (Fed. Cir. Aug. 15, 2019).

[2] Holland Furniture Co. v. Perkins Glue Co., 277 U.S. 245 (1928).

[3] General Electric Co. v. Wabash Appliance Corp., 304 U.S. 364 (1934).