United States Court of Appeals for the Federal Circuit

SHIRE DEVELOPMENT, LLC, SHIRE PHARMACEUTICAL DEVELOPMENT, INC., COSMO TECHNOLOGIES LIMITED, GIULIANI INTERNATIONAL LIMITED, NKA NOGRA PHARMA LIMITED,
Plaintiffs-Appellees

v.

WATSON PHARMACEUTICALS, INC., NKA ACTAVIS, INC., WATSON LABORATORIES, INC. - FLORIDA, NKA ACTAVIS LABORATORIES FL, INC., WATSON PHARMA, INC., NKA ACTAVIS PHARMA, INC., WATSON LABORATORIES, INC.,
Defendants-Appellants

2016-1785

Appeal from the United States District Court for the Southern District of Florida in No. 0:12-cv-60862-DMM, Judge Donald M. Middlebrooks.

Decided: February 10, 2017

EDGAR HAUG, Frommer Lawrence & Haug LLP, New York, NY, argued for plaintiffs-appellees. Also represented by ELIZABETH MURPHY, ERIKA SELLI, JASON AARON LIEF, ANDREW S. WASSON.

STEVEN ARTHUR MADDOX, Maddox Edwards, PLLC, Washington, DC, argued for defendants-appellants. Also represented by JEREMY J. EDWARDS, KAVEH SABA.

Before PROST, *Chief Judge,* TARANTO and HUGHES, *Circuit Judges.*

HUGHES, *Circuit Judge*.

Plaintiffs (collectively, Shire) sued Defendants (collectively, Watson) for infringing claims 1 and 3 of U.S. Patent No. 6,773,720 by filing Abbreviated New Drug Application No. 203817 with the Food and Drug Administration seeking to market a generic version of Shire's mesalamine drug, LIALDA®. Because Watson's ANDA Product does not satisfy the Markush group requirements in claim 1(b), we reverse and remand with instructions to enter judgment of non-infringement.

I

A

The '720 patent is directed to a controlled-release oral pharmaceutical composition of mesalamine (also known as mesalazine or 5-amino-salicylic acid) used to treat certain inflammatory bowel diseases. *Shire Dev., LLC v. Watson Pharm., Inc.*, 787 F.3d 1359, 1361 (Fed. Cir. 2015) (2015 Decision). That composition includes the mesalamine active ingredient; an inner, lipophilic matrix; an outer, hydrophilic matrix; and other optional excipients. '720 patent col. 2 ll. 36–44.

When a matrix is hydrophilic, it "has an affinity for water" and therefore "readily dissolves in" it. 2015 Decision, 787 F.3d at 1362 n.1; *see Shire Dev. LLC v. Watson Pharm., Inc.*, No. 12-60862-CIV, 2016 WL 1258885, at *6 (S.D. Fla. Mar. 28, 2016) (2016 Trial Decision) (noting the parties' stipulated-to definition of "hydrophilic" as "having

an affinity to water"). Conversely, when a matrix is lipophilic, it "has an affinity for lipids" and therefore "resists dissolving in water." 2015 Decision, 787 F.3d at 1362 n.1; *see id.* at 1365 (noting the parties' stipulated-to definition of "lipophilic" as "poor affinity towards aqueous fluids").

Shire asserts claims 1 and 3 of the '720 patent. In relevant part, claim 1 reads:

> 1. Controlled-release oral pharmaceutical compositions containing as an active ingredient 5-amino-salicylic acid, comprising:
>
> > a) an *inner lipophilic matrix* consisting of *substances selected from the group consisting of* unsaturated and/or hydrogenated fatty acid, salts, esters or amides thereof, fatty acid mono-, di- or triglycerids, waxes, ceramides, and cholesterol derivatives with melting points below 90° C., and wherein the active ingredient is dispersed both in said [sic] the lipophilic matrix and in the hydrophilic matrix;
> >
> > b) an *outer hydrophilic matrix* wherein the lipophilic matrix is dispersed, and said outer hydrophilic matrix *consists of compounds selected from the group consisting of* polymers or copolymers of acrylic or methacrylic acid, alkylvinyl polymers, hydroxyalkyl celluloses, carboxyalkyl celluloses, polysaccharides, dextrins, pectins, starches and derivatives, alginic acid, and natural or synthetic gums;
> >
> > c) optionally other excipients . . . .

'720 patent col. 6 ll. 7–30 (emphases added). Dependent claim 3 limits the composition to "the form of tablets, capsules, [or] mintablets [sic]." *Id.* col. 6 ll. 34–35.

B

In 2013, following a bench trial, the district court rejected Watson's invalidity arguments that the '720 patent lacked written description and enablement, and held that Watson infringed claims 1 and 3. *Shire Dev. LLC v. Watson Pharm., Inc.*, No. 12-60862-CIV, 2013 WL 1912208, at *16 (S.D. Fla. May 9, 2013) (2013 Trial Decision).

On appeal, and again after remand from the Supreme Court, we held that the '720 patent matrices are "defined by mutually exclusive spatial characteristics—one inner, one outer—and mutually exclusive compositional characteristics—one hydrophilic, one lipophilic." 2015 Decision, 787 F.3d at 1366, *remanded by* 135 S. Ct. 1174 (2015), *granting cert. to and vacating* 746 F.3d 1326 (Fed. Cir. 2014). Thus we concluded that a "matrix—not just an excipient within the matrix"—must exhibit the appropriate characteristic. *Id.* at 1365 (emphasis omitted). We further explained that the matrix compositions are "limited by the Markush groups" added during prosecution "to overcome the examiner's rejection of the claims as obvious." *Id.* at 1367.

Summarizing the operation of the Markush groups in the '720 patent, we determined that "the correct construction requires that the inner volume contain substances from the group described for the inner lipophilic matrix (which are all lipophilic substances), and that the outer volume separately contain substances from the group described for the outer hydrophilic matrix (which are all hydrophilic)." *Id.*

On remand, the district court concluded that Watson's ANDA Product satisfied the "inner lipophilic matrix" and "outer hydrophilic matrix" limitations. *See* 2016 Trial Decision, 2016 WL 1258885, at *4, *15. The court also determined that Watson's ANDA Product satisfied the Markush limitations because the excipients falling out-

side the respective Markush groups were "unrelated" to the invention since they did not drive the water-affinity property of their respective matrices. *Id.* at *15. Watson appeals the district court's constructions of "inner lipophilic matrix" and "outer hydrophilic matrix" and its findings of infringement. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

II

"Following a bench trial, we review a district court's conclusions of law *de novo* and its findings of fact for clear error." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1303 (Fed. Cir. 2015).

"A Markush claim is a particular kind of patent claim that lists alternative species or elements that can be selected as part of the claimed invention." *Multilayer Stretch Cling Film Holdings, Inc. v. Berry Plastics Corp.*, 831 F.3d 1350, 1357 (Fed. Cir. 2016). This typically appears in the form: "a member selected from the group consisting of A, B, and C." 2015 Decision, 787 F.3d at 1363 n.3 (quoting *Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1372 (Fed. Cir. 2005)).

Here, claim 1's (a) and (b) limitations use the phrase "consisting of," or "consists of," to characterize the matrix, and "consisting of" to define the groups, which "creates a very strong presumption that that claim element is 'closed' and therefore 'exclude[s] any elements, steps, or ingredients not specified in the claim.'" *Multilayer Stretch Cling Film Holdings*, 831 F.3d at 1358 (quoting *AFG Indus., Inc. v. Cardinal IG Co.*, 239 F.3d 1239, 1245 (Fed. Cir. 2001)). Overcoming this presumption requires "the specification and prosecution history" to "unmistakably manifest an alternative meaning," such as when the patentee acts as its own lexicographer. *Id.* at 1359; *see Conoco, Inc. v. Energy & Envtl. Int'l*, 460 F.3d 1349, 1359 n.4 (Fed. Cir. 2006).

Though the "consisting of" presumption is very strong, we permit the rare exception for "aspects unrelated to the invention." *Norian Corp. v. Stryker Corp.*, 363 F.3d 1321, 1331 (Fed Cir. 2004). In *Norian*, we considered whether adding a spatula to a calcium phosphate chemical kit designed to repair teeth and bones took the accused product outside the scope of the asserted patent. *Id.* at 1324, 1331–32. The claim at issue contemplated only aspects of the chemicals themselves:

> 8. A kit for preparing a calcium phosphate mineral, said kit consisting of:
>
> > at least one calcium source and at least one phosphoric acid source free of uncombined water as dry ingredients; and
> >
> > a solution consisting of water and a sodium phosphate, where the concentration of said sodium phosphate in said water ranges from 0.01 to 2.0 M and said solution has a pH in the range of about 6 to 11.

Id. at 1324–25. We concluded that "[i]nfringement is not avoided by the presence of a spatula, for the spatula has no interaction with the chemicals, and is irrelevant to the invention." *Id.* at 1332.

Here, Watson's ANDA Product does not facially satisfy the claim 1(b) Markush limitation. The Watson ANDA Product's extragranular space—which the district court recognized is the outer hydrophilic matrix—contains the following excipient composition and properties:

Excipient	Amount (mg)	Property
SSG	<34 (unknown)	Hydrophilic
Magnesium stearate	<7 (unknown)	Lipophilic
Colloidal silicon dioxide	4	

Watson's Opening Br. at 16, *see* J.A. 2162, 2209.[1] As the district court concluded, "[m]agnesium stearate, an excipient not within the claim 1(b) Markush group, is present within the extragranular space." *See* 2016 Trial Decision, 2016 WL 1258885, at *15. So the claim 1(b) limitation is literally violated.

Nonetheless, the district court found that Watson infringed because the component outside of the Markush group—i.e., the lipophilic magnesium stearate in the hydrophilic outer matrix—is unrelated to the invention. Therefore, the district court held that the lipophilic component in the outer hydrophilic matrix fell within the exception announced in *Norian*. *Id.* at *14–15. We disagree with the district court's interpretation of *Norian* and what constitutes a component unrelated to the invention.

The putative invention of the '720 patent is a multi-matrix system that relies on the hydrophilic and lipophilic characteristics of the matrices to release mesalamine in the colon "in a sustained and uniform manner." 2015 Decision, 787 F.3d at 1362. When the outer, hydrophilic matrix interacts with a person's digestive fluids, the matrix creates a swollen barrier preventing aqueous solution from reaching the inner, lipophilic matrix. *See* '720 patent col. 2 ll. 60–64. This delay permits the product to proceed through the digestive system until the water breaks apart the outer matrix, releasing the lipophilic granules. *See id.* col. 3 l. 57–col. 4 l. 5.

Here, the district court concluded that the "magnesium stearate in the extragranular space is *overwhelmed* by the hydrophilic properties of the sodium starch glycolate in the extragranular space" and credited expert testimony that the hydrophilic "sodium starch glycolate is *more*

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[1] SSG is an abbreviation for sodium starch glycolate.

potent than the mag stearate" when "outside" the granules. 2016 Trial Decision, 2016 WL 1258885, at *15 (emphases added) (internal quotation marks omitted). The district court thereby found that the magnesium stearate exerted lipophilic influence in the outer matrix, and that finding is well supported: Shire's expert acknowledged that "the magnesium stearate in the spaces between the granules is no less lipophilic than the magnesium stearate in the granules," *see* J.A. 1157, and the court found that magnesium stearate is so strongly lipophilic that it may "impart lipophilic characteristics to a composition even in low concentrations," 2016 Trial Decision, 2016 WL 1258885, at *11; *see id.* at *11–12 (crediting expert testimony that magnesium stearate "is one of the most lipophilic things [the expert could] imagine," and explaining that a concentration of 0.5% magnesium stearate could increase dissolution time by more than tenfold). No one has suggested that magnesium stearate, when in the outer matrix, is neither lipophilic nor hydrophilic. Thus, we conclude that, based on the district court's findings, the magnesium stearate retains its lipophilic character in the extragranular space. Accordingly, the magnesium stearate structurally and functionally relates to the invention, and its presence in the outer matrix violates the "consisting of" requirement in claim 1(b).

Shire argues, and the district court held, that the magnesium stearate in Watson's product—which Watson includes as a lubricant rather than for its lipophilic properties—is unrelated to the invention because it is not sufficiently lipophilic to render the outer matrix lipophilic. But *Norian* did not restrict "related" components to only those that advance or are intended to advance a Markush group's allegedly inventive elements. And we decline to impose such a requirement, which would in effect equate the scope of a Markush group's "consisting of" language with either "comprising" or "consisting essentially of"

language. *See CIAS, Inc. v. Alliance Gaming Corp.*, 504 F.3d 1356, 1360 (Fed. Cir. 2007) ("'[C]omprising' . . . is inclusive or open-ended and does not exclude additional, unrecited elements or method steps . . . ." (quoting *Georgia-Pacific Corp. v. U.S. Gypsum Co.*, 195 F.3d 1322, 1327–28 (Fed. Cir. 1999)); *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1239 (Fed. Cir. 2003) ("The phrase 'consisting essentially of' . . . permit[s] inclusion of components not listed in the claim, provided that they do not 'materially affect the basic and novel properties of the invention.'" (quoting *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998)).

Shire also argues that we must interpret claim 1(b) to cover products with magnesium stearate in the extragranular space because the '720 patent examples disclose magnesium stearate in the outer matrix. Assuming that Shire is correct about the content of the examples, we still find that Shire has not "overcome the exceptionally strong presumption" that Markush groups are closed. *Multilayer Stretch Cling Film Holdings*, 831 F.3d at 1359 (holding that a patent specification's listing of components not listed in a Markush group was insufficient to overcome the presumption created by "consisting of" claim language). Shire does not challenge the district court's construction of "consisting of," and neither the '720 patent specification nor the prosecution history reflect intent to adopt a meaning of "consisting of" other than the well-established, limited definition. Thus, we apply the plain claim language.[2]

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[2] The district court's reliance on claim 1(c), which recites "optionally other excipients," is erroneous. 2016 Trial Decision, 2016 WL 1258885, at *15 n.15. Claim 1(c) plainly falls under the preamble's "comprising" transitional phrase and outside of claim 1's (a) and (b) Markush

Accordingly, we conclude that Watson's ANDA Product does not satisfy the claim 1(b) Markush limitation, and, by extension, does not satisfy dependent claim 3. *See Ferring B.V. v. Watson Labs., Inc.-Florida*, 764 F.3d 1401, 1411 (Fed. Cir. 2014) ("One who does not infringe an independent claim cannot infringe a claim dependent [on] (and thus containing all the limitations of) that claim." (quoting *Wahpeton Canvas Co. v. Frontier, Inc.,* 870 F.2d 1546, 1552 n.9 (Fed. Cir. 1989)).[3] We reverse the district court's judgment and remand for entry of judgment of non-infringement and other proceedings consistent with this opinion.

REVERSED AND REMANDED

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groups. Claim 1(c) therefore does not present a permissive catch-all to those closed Markush groups.

[3] Because this conclusion resolves the appeal, we do not address Watson's other claim construction or non-infringement arguments.