United States Court of Appeals for the Federal Circuit

POZEN INC.,
Plaintiff-Appellee,

v.

PAR PHARMACEUTICAL, INC.,
Defendant-Appellant,

AND

DR. REDDY'S LABORATORIES, INC.,
Defendant-Appellant,

AND

ALPHAPHARM PTY LTD.,
Defendant-Appellant.

2011-1584, -1585, -1586

Appeal from the United States District Court for the Eastern District of Texas in Consolidated Case Nos. 08-CV-0437, 09-CV-0003, and 09-CV-0182, Judge Leonard Davis.

Decided: September 28, 2012

STEPHEN M. HASH, Vinson & Elkins LLP, of Austin, Texas, argued for plaintiff-appellee. With him on the

brief were TRACEY B. DAVIES, WILLEM G. SCHUURMAN and JENNIFER LIBRACH NALL; and STEPHANIE LOLLO DONAHUE and REBECCA J. CANTOR, of New York, New York.

RICHARD J. BERMAN, Arent Fox LLP, of Washington, DC, argued for defendant-appellants Par Pharmaceutical, Inc. and Alphapharm Pty., Ltd. Of counsel on the brief was THOMAS J. PARKER, Alston & Bird, LLP, of New York, New York. Of counsel for Par Pharmaceutical, Inc. were TANIEL ERMANO ANDERSON, TIMOTHY BUCKNELL, AZIZ BURGY, JANINE A. CARLAN, JOSHUA T. MORRIS and AMY E. LIGLER SCHOENHARD. Of counsel for Alphapharm Pty., Ltd., was NATALIE C. CLAYTON, Alston & Bird, LLP, of New York, New York.

PAUL H. KOCHANSKI, Lerner, David, Littenberg, Krumholz & Mentlik, LLP, of Westfield, New Jersey, argued for defendant-appellant, Dr. Reddy's Laboratories, Inc. With him on the brief were MICHAEL H. TESCHNER and ROY H. WEPNER.

Before NEWMAN, CLEVENGER, and WALLACH, *Circuit Judges*.

Opinion for the court filed by *Circuit Judge* WALLACH. Dissenting-in-part opinion filed by *Circuit Judge* CLEVENGER.

WALLACH, *Circuit Judge*.

INTRODUCTION

Par Pharmaceutical, Inc. ("Par"), Alphapharm Pty Ltd. ("Alphapharm"), and Dr. Reddy's Laboratories, Inc. ("DRL") (collectively "Appellants") appeal from the final judgment of the United States District Court for the Eastern District of Texas. Following a bench trial, the

district court determined that the asserted claims of U.S. Patent No. 6,060,499 (filed Sept. 11, 1998) (the "'499 patent"), U.S. Patent No. 6,586,458 (filed Apr. 27, 2000) (the "'458 patent"), and U.S. Patent No. 7,332,183 (filed Dec. 22, 2003) (the "'183 patent") (collectively "patents-in-suit") are not invalid as obvious under 35 U.S.C. § 103. The district court also found that the patents-in-suit were infringed by Par and DRL's Abbreviated New Drug Application ("ANDA") filings. As a result, Par and DRL were enjoined from making, using, importing, selling or offering to sell their generic products in the United States.[1] We affirm the district court's decision because it did not err in finding the patents-in-suit not invalid and infringed.

BACKGROUND

Pozen developed a method for treating migraines by combining two drugs, sumatriptan and naproxen, in a single tablet. *Pozen Inc. v. Par Pharm., Inc.*, 800 F. Supp. 2d 789, 796 (E.D. Tex. 2011). Sumatriptan, a 5-HT receptor agonist, was developed in the late 1980s and is widely accepted as an effective medicine for migraines, but it does not prevent the reoccurrence of migraine symptoms. *Id.* at 797. Naproxen is a well known nonsteriodal anti-inflammatory drug ("NSAID"). *Id.* at 798. Pozen, in partnership with GlaxoSmithKline ("GSK"), markets a combination of sumatriptan and naproxen called Trexi-

[1] After the district court issued its final claim construction order, Pozen stipulated to a judgment of non-infringement of the '183 patent in favor of Alphapharm. Therefore, Alphapharm's interest in this appeal is limited to the validity of the '499 and '458 patents. Pozen also sued Teva Pharmaceuticals USA, Inc. ("Teva") for patent infringement on the basis of Teva's ANDA, but the parties settled before trial. *Pozen Inc. v. Par Pharm., Inc.*, 800 F. Supp. 2d 789, 796 n.1 (E.D. Tex. 2011).

met® and holds three related patents relevant to this appeal. *Id.* The '499 patent claims a method of treating migraines comprising co-timely administration of 5-HT agonists and long-acting NSAIDs. '499 patent col.1 ll.13-17. The '458 patent is a continuation of the '499 patent and claims methods and compositions combining 5-HT agonists and long-acting NSAIDs. '458 patent col.1 ll.18-20. The '183 patent claims a multilayer pharmaceutical tablet with a triptan, such as sumatriptan, and a NSAID in separate layers that dissolve independently. '183 patent col.1 ll.54-57.

Pozen filed a New Drug Application ("NDA") to market Treximet® and obtained approval from the United States Food and Drug Administration ("FDA") on April 15, 2008. *Pozen*, 800 F. Supp. 2d at 798. Pozen listed the patents-in-suit in its NDA as covering Treximet®. The patents are included in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (known as "the Orange Book"), *see* 21 U.S.C. § 355(b)(1), indicating they could be infringed by the unlicensed manufacture, use, or sale of Treximet®. *Pozen*, 800 F. Supp. 2d at 798.

Appellants are generic pharmaceutical manufacturers who filed ANDAs with the FDA seeking approval to market generic forms of Treximet® before the expiration of Pozen's patents. *Id.*; *see* 21 U.S.C. § 355(b)(2), (j)(2). Appellants filed their application certifying that the patents listed in the Orange Book are "invalid or will not be infringed" by the generic products. 21 U.S.C. § 355(j)(2)(A)(vii)(IV); *Pozen*, 800 F. Supp. 2d at 798-99; Such a certification constitutes an artificial act of infringement. 35 U.S.C. § 271(e)(2); *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003). Thereafter, Pozen filed complaints against Appellants for infringement of claim 15 of the '499 patent; claims 11, 12, 24, 26, 27, 29, and 30 of the '458 patent; and claim 2 of the

'183 patent under the Hatch-Waxman Act.[2] 35 U.S.C. § 271(e)(2)(A); *Pozen*, 800 F. Supp. 2d at 799.

A. The Relevant '499 Patent Claims

The district court found Appellants' ANDA products directly infringe Claim 15 of the '499 patent, which depends on claim 5 and reads:

> 5. A therapeutic package for dispensing to, or for use in dispensing to, a migraine patient, which comprises:
>
> (a) one or more unit doses, each such unit dose comprising:
>
> (i) a 5-HT agonist and
>
> (ii) a long-acting, non-steroidal, anti-inflammatory drug (LA-NSAID);
>
> wherein the respective amounts of said 5-HT agonist and said LA-NSAID in said unit dose are effective, upon concomitant administration to said patient of one or more of said unit doses, to reduce migraine relapse or produce longer lasting efficacy

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[2] It is "an act of infringement to submit . . . an application" for approval from the FDA to manufacture "a drug claimed in a patent." 35 U.S.C. § 271(e)(2)(A). Section 271(e)(2)(A) provides that an ANDA constitutes an artificial act of infringement for which the applicant may be liable. *Warner-Lambert*, 316 F.3d at 1365. It "creates case-or-controversy jurisdiction to enable the resolution of an infringement dispute before the ANDA applicant has actually made or marketed the proposed product." *Id.*; *see Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997). The determination under § 271 is the same as any other infringement suit to inquire whether a product would infringe a patent if the ANDA product was on the market. *Warner-Lambert*, 316 F.3d at 1365.

> compared to the administration of said 5-HT agonist in the absence of said LA-NSAID or the administration of said LA-NSAID in the absence of said 5-HT agonist, and
>
> (b) a finished pharmaceutical container therefor, said container containing said unit dose or unit doses, said container further containing or comprising labeling directing the use of said package in the treatment of migraine.
>
> . . . .
>
> 15. The improvement, method, or composition of claims 1, 2, 3, 4, 5, 6, 7, or 8, wherein said 5-HT agonist is sumatriptan, said LA-NSAID is naproxen and the unit dosage form is an oral unit dosage form comprising sumatriptan in an amount greater than 15 mg, and naproxen in an amount greater than 200 mg.

'499 patent col.14 ll.1-19; col.15 ll.12-17.

B. The Relevant '458 Patent Claims

The district court found Appellants' ANDA products directly infringe claims 11, 12, and 24, which depend on claim 3, as well as claims 26, 27, 29, and 30, which specify sumatriptan is the 5-HT agonist and naproxen is the LA-NSAID used in various dosages. *Pozen*, 800 F. Supp. 2d at 806. Representative claim 3 states:

> 3. A pharmaceutical composition in unit dosage form, useful in treating a migraine headache patient, which comprises:
>
> (a) a 5-HT agonist, wherein said 5-HT agonist is a triptan; and
>
> (b) a long-acting, non-steroidal, anti-inflammatory drug (LA-NSAID),

> wherein said LA-NSAID has a pharmacokinetic half-life of at least 4 hours and a duration of action of at least 6 hours;
>
> wherein the respective amounts of said 5-HT agonist and said LA-NSAID in said composition are effective, upon concomitant administration to said patient of one or more of said unit dosage forms of said composition, to produce longer lasting efficacy compared to the administration of said 5-HT agonist in the absence of said LA-NSAID or the administration of said LA-NSAID in the absence of said 5-HT agonist.

'458 patent col.12 ll.29-45.

C. The Relevant '183 Patent Claims

The district court held that under the doctrine of equivalents Par and DRL's ANDA products infringe claim 2 of the '183 patent, which is dependent on claim 1, and reads:

> 1. A multilayer pharmaceutical tablet comprising naproxen and a triptan and, wherein:
>
> a) substantially all of said triptan is in a first layer of said tablet and substantially all of said naproxen is in a second, separate layer; and
>
> b) said first layer and said second layer are in a side by side arrangement such that the dissolution of said naproxen occurs independently of said triptan.
>
> 2. The tablet of claim 1, wherein said naproxen is in the form of naproxen sodium between 200 and 600 mg.

'183 patent col.18 ll.30-39. The court construed the phrase "substantially all of said triptan is in a first layer

of said tablet and substantially all of said naproxen is in a second, separate layer" as meaning "[a]t least 90%, and preferably greater than 95%, of the total triptan present in the tablet is included within one distinct layer and at least 90%, and preferably greater than 95%, of the naproxen present in the tablet is included within a second distinct layer." *Pozen*, 800 F. Supp. 2d at 809. The parties agreed that the claim term "dissolution of said naproxen occurs independently of said triptan" means "[d]issolution of naproxen . . . and triptan from the multilayer tablet . . . occurs in the same amount of time ± 10% as when the same amount of naproxen . . . and triptan are given separately." Joint Appendix ("J.A.") 653.

D. Procedural History

Based on the ANDA filings, Pozen filed suit against Appellants for infringement of the '499, '458, and '183 patents and asked for a permanent injunction against Appellants from making, using, selling, offering to sell or importing into the United States their ANDA products until the patents-in-suit expire. *Pozen*, 800 F. Supp. 2d at 799. The lawsuit triggered a 30-month stay of FDA approval for Appellants' ANDAs. *Id.*

Following the claim construction hearing, the district court conducted a five-day bench trial regarding Pozen's infringement claims and Appellants' noninfringement, invalidity, and unenforceability defenses and counter-claims. The district court held, in part, that the patents were not invalid because they were neither anticipated nor obvious in light of the prior art, that Appellants' ANDA products infringed the '499 and '458 patents, and that Par and DRL's ANDA products infringed the '183 patent. *Id.* Furthermore, the district court held that the '499 patent claims asserted were not invalid due to lack of written description. *Id.* at 821-22. Accordingly, the dis-

trict court enjoined Par, Alphapharm, and DRL from making or selling their respective ANDA products. *Id.* at 826. Par, Alphapharm, and DRL filed a timely appeal.[3] We have jurisdiction over the appeals pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

A. Standard of Review

This court reviews judgments of the district court after a bench trial "for errors of law and clearly erroneous findings of fact." *Zenon Envtl., Inc. v. U.S. Filter Corp.*, 506 F.3d 1370, 1377 (Fed. Cir. 2007) (citations and internal quotation marks omitted).

Appellants challenge the validity of the '499 and '458 patents in light of four prior art references.[4] Appellants also challenge the validity of the '183 patent in light of the

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[3] Par and Alphapharm filed a joint brief, Brief for Defendants-Appellants Par Pharmaceutical, Inc. and Alphapharm Pty Ltd. ("Par's Br.") and DRL submitted a separate brief, Brief for Defendant-Appellant Dr. Reddy's Laboratories, Inc. ("DRL's Br."), adopting in accordance with Fed. R. App. P. 28(i) Par and Alphapharm's arguments with regard to invalidity of the '499, '458, and '183 patents over the prior art, DRL's Br. at 1.

[4] The following references will be discussed below: Parma, E., et al., *The Treatment of Migraine: A Study in General Medicine*, 11 Ricerca & Practica 1995, at 64 ("Parma"); Saadah, H., *Abortive Migraine Therapy With Oral Naproxen Sodium Plus Metoclopramide Plus Ergotamine Tartrate With Caffeine*, 32 Headache 1992, at 95 ("Saadah"); Raskin, N., *Acute and Prophylactic Treatment of Migraine: Practical Approaches and Pharmacologic Rationale*, 43 Neurology, June 1993, at 839 ("Raskin"); Henry Ford Hospital, Patient Records; Catarci et al., *Ergotamine-Induced Headache Can Be Sustained By Sumatriptan Daily Intake*, 14 Cephalalgia 1994, at 374 ("Catarci").

'499 patent and prior art.[5] Appellants ask this court to hold the '499 patent invalid for lack of written description. Additionally, Appellants challenge the district court's infringement determination as to the '183 patent. We address each argument in turn.

B. Invalidity

1. *The '499 And '458 Patents Are Not Obvious*

A party asserting invalidity must present clear and convincing evidence to overcome a patent's presumption of validity. 35 U.S.C. § 282; *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2245 (2011). A patent claim is invalid as obvious "when 'the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. . . .'" *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007) (quoting 35 U.S.C. § 103(a)). To determine if a patent is obvious the district court looks to: (1) the scope and content of the prior art; (2) differences between the prior art and the claims; (3) the level of ordinary skill in the art; and (4) secondary considerations such as commercial success and failure of others. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). "'Obviousness is a question of law, reviewed *de novo*, based upon underlying factual questions which are reviewed for clear error following a bench trial.'" *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293, 1300 (Fed. Cir. 2007) (quoting *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006)).

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[5] Bandelin, R., *Compressed Tablets by Wet Granulation*, 179 Herbert Lieberman et al. eds. (2d ed. 1989) ("Bandelin").

The district court found that the prior art references did not invalidate the '499 and '458 patents. Specifically, the district court reasoned that the references did not, separately or combined, "teach or suggest the simultaneous administration of sumatriptan and naproxen. Nor . . . otherwise disclose to one of ordinary skill in the art that the combination of sumatriptan and naproxen produces a longer lasting efficacy reducing migraine relapse compared to the administration of naproxen or sumatriptan alone." *Pozen*, 800 F. Supp. 2d at 819.

As an initial matter, Par argues that the district court erred because it failed to apply the term "concomitant administration" to include simultaneous and sequential administration as it had been construed. If the district court had applied the terms as construed, Par asserts, it would have found the '499 and '458 patents invalid because the prior art showed concomitant administration.

Within the context of the claim language the district court properly applied its claim construction. In its obviousness analysis the district court only referred directly to whether the references disclosed "simultaneous administration," rather than using the broader term "concomitant administration." *See Pozen*, 800 F. Supp. 2d at 814-19. The district court construed the term "concomitantly administering" in the '499 patent claims as:

> Simultaneous administration; or administration of a second drug for migraine relief while a first drug for migraine relief is present in a therapeutically effective amount; or administration of a 5-HT agonist and NSAID such that the effective plasma levels of the NSAID will be present in a subject from about one hour to about 12-24 hours after the onset of migraine or onset of precursor symptoms of a migraine.

J.A.2554. The district court construed the term "concomitantly administering" in the '458 patent claims as "[g]iven in close enough temporal proximity to allow their individual therapeutic effects to overlap." J.A.2555. None of the parties contested the claim construction. Before the bench trial the parties agreed that the claim terms "unit dose form," "unit doses," and "unit dosage form(s)" in both the '499 and '458 patents meant "single drug administration entity(ies)." Every asserted claim in the '499 and '458 patents contains the "unit dose" limitation. *See* '499 patent col.14 ll.1-15; '458 patent col.12 ll.29-45. When considering the claim language as a whole the term "unit dose" necessarily limits concomitant administration to mean simultaneous administration because a single drug administration entity cannot be administered in any other fashion. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (en banc) ("[T]he context in which a term is used in the asserted claim can be highly instructive."). Therefore, the district court properly limited its analysis of the prior art to whether the references taught simultaneous administration of naproxen and sumatriptan.

Appellants further argue that the '499 and '458 patents should be invalid as obvious in light of the prior art, asserting that references Parma, Saadah, patient records from Henry Ford Hospital, or Catarci, alone or in combination, teach a "concomitant administration" of sumatriptan and naproxen to treat migraines. If the district court had followed the case law and applied the claim construction, Appellants contend, it would have found both the '499 and '458 patents invalid. We consider each reference in turn.

i. *The Parma Reference*

The district court determined that the Parma reference does not render the '499 and '458 patents obvious.

Pozen, 800 F. Supp. 2d at 815-16. We agree. Parma is an epidemiological survey assessing various migraine treatments entitled, "The Treatment Of Migraine: A Study In General Medicine."[6] One of the tables, labeled "Table VI.

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[6] At trial, Pozen presented, and the district court allowed into evidence, a declaration from one of the co-authors of the Parma reference, referred to as the "Tognoni declaration," which stated:

> While my article speaks of [combination therapy] of many pairs of drugs, including NSAIDs and sumatriptan, this is not meant as a reference to administering those two drugs at the same time. . . . it refers to the common practice of that time of migraine patients taking drugs separately in sequence, with a required gap in time between administrations of the drugs to determine the efficacy of the first drug before trying additional drugs.

J.A.158512.

DRL argues that the declaration is inadmissible as hearsay and irrelevant, and in admitting it the district court abused its discretion. DRL's Br. at 52. Pozen argues that the declaration is admissible under the residual hearsay rule, Fed. R. of Evid. 807. *See* Pozen's Br. at 30. We review evidentiary determinations under the law of the regional circuit. *Lexion Med. v. Northgate Techs., Inc.*, 641 F.3d 1352, 1358 (Fed. Cir. 2011). The Fifth Circuit reviews decisions to admit or exclude evidence for abuse of discretion. *United States v. Phillips*, 219 F.3d 404, 409 (5th Cir. 2000). "The residual hearsay exception is to be used only rarely, in truly exceptional cases." *United States v. Walker*, 410 F.3d 754, 757 (5th Cir. 2005) (citations and internal quotation marks omitted). To admit evidence under the residual hearsay rule, there must be at least circumstantial guarantees of trustworthiness. *Id.* at 758. The Fifth Circuit has found there are equivalent circumstantial guarantees of trustworthiness when the declaration is made under oath and the declarant is subject to the penalties of perjury, the testimony was preserved on videotape, and the witnesses were subject to cross-examination. *Id.* Here, Tognoni made a written state-

Combinations: 2 drugs," listed "FANS + sumatriptan" (FANS is the Italian abbreviation for NSAIDs) among fifteen other drug combinations for the treatment of migraines. Another table, labeled "Table VIII. 'Unsatisfactory' treatments," lists percentages of patients unsatisfied with various monotherapy treatments; included in that list is "sumatriptan."

Table VI. Combinations: 2 drugs (53 cases, type 1 and 2)	
FANS + flunarizine	13
FANS + antiemetics	5
FANS + antidepressants	6
FANS + ergotamines	2
FANS + analgesics	2
FANS + sumatriptan	2
FANS + FANS	1
FANS + other drugs	1
Ergotamines + benzodiazepine	1
Ergotamines + antidepressants	1

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ment under penalty of perjury, but was never subjected to cross-examination, which may be enough under Fifth Circuit law to guarantee trustworthiness. However, even if it is trustworthy, this is not an exceptional case and thus does not warrant the residual hearsay exception. *See Ortho-McNeil Pharm., Inc. v. Mylan Labs, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008).

Ergotamines + other drugs	3
Sumatriptan + flunarizine	2
Sumatriptan + beta-blockers	1
Analgesic + analgesic	2
Various combinations	11

J.A.242118.

Table VIII. "Unsatisfactory" treatments (migraine type 1 and 2)			
	Monotherapy	**Unsatisfactory treatments**	**%**
FANS	118	44	37.9
Sumatriptan	37	16	43.2
Analgesics	89	49	66.0
Ergotamine derivatives	18	14	77.7

J.A.242119.

Appellants' expert testified that Parma teaches simultaneous administration of various drug combinations, and someone skilled in the art would look at "Table VIII. 'Unsatisfactory' treatments" and be motivated to either administer another agent or administer a combination therapy. *Pozen*, 800 F. Supp. 2d at 816. The district court gave more weight to Pozen's expert who testified that a person skilled in the art would have interpreted Parma to disclose a sequential administration of various drug

combinations. *Id.* As the tables reproduced above illustrate, Parma revealed the types of treatments used and documented the number of unsatisfactory treatments reported. Parma only specifies the unsatisfactory results of monotherapy treatment in Table VIII; it does not indicate the relative successes of various combination treatments listed in Table VI.[7] Furthermore, the district court found that Parma does not disclose anything about the combination of "FANS + sumatriptan" in particular reducing migraine relapse or producing longer lasting efficacy, nor does it disclose the dosage of the combination treatment. *Id.* Although the district court abused its discretion by admitting the Tognoni declaration, *see supra* 13 n.6, it was harmless error, there was not clear and convincing evidence that the '499 and '458 patents are obvious over the Parma reference.

ii. *The Saadah Reference*

The Saadah reference is a 1992 report entitled "Abortive Migraine Therapy With Oral Naproxen Sodium Plus Metoclopramide Plus Ergotamine Tartrate With Caffeine." It discloses the simultaneous delivery of several components: ergotamine, which is a 5-HT agonist that at the time was a widely used anti-migraine agent; metoclopramide and caffeine to reduce nausea and improve "gastric emptying" which in turn leads to better absorption of anti-migraine agents; and naproxen for its pain and inflammation reduction effects.

Par argues that another article, N.H. Raskin's "Acute and Prophylactic Treatment of Migraine: Practical Approaches and Pharmacologic Rationale," ("Raskin") shows

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[7] Although the properties of the two agents were known independently, Parma does not give any indication that the combination of the two produced any benefit beyond those experienced when each agent is taken alone.

sumatriptan has beneficial effects on nausea, and can be used instead of ergotamine to treat migraines eliminating the need for a concurrent antiemetic.[8] Therefore, Appellants contend, a person of ordinary skill in the art would reasonably expect to successfully substitute sumatriptan for ergotamine, both 5-HT agonists, in the treatment plan disclosed by Saadah. Furthermore, Appellants contend that in substituting sumatriptan for ergotamine, there would no longer be a need for antiemetics, so metoclopramide and caffeine would be unnecessary. Accordingly, Appellants assert, Saadah and Raskin together teach the simultaneous administration of sumatriptan and naproxen, rendering the '499 and '458 patents obvious.

Pozen contends that a person of ordinary skill in the art motivated to substitute sumatriptan for ergotamine would remove not only metoclopramide and caffeine from the treatment plan but also naproxen because sumatriptan was recognized to have analgesic and anti-inflammatory effects. Therefore, Pozen argues, the formulation would result in sumatriptan monotherapy.

The district court held that after reading Saadah, it is not obvious that one could substitute sumatriptan for ergotamine and remove metoclopramide and caffeine as unnecessary. *Pozen*, 800 F. Supp. 2d at 817. We agree. Saadah disclosed each drug as having a specific purpose, and even though Raskin teaches that antiemetics are unnecessary with sumatriptan, Raskin does not provide the motivation to a skilled artisan to substitute one agent in place of three. Nor does Saadah teach the remaining efficacy limitations, since it gives no reason to assume that an entirely different combination of agents would

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[8] Raskin teaches that sumatriptan can be used as an anti-migraine without the concurrent use of anti-nausea agents. J.A.241903.

have the same success as the combination disclosed, nor does it disclose the combination therapy has any added benefits over any of the components given individually. *See Crocs, Inc. v. Int'l Trade Comm'n*, 598 F.3d 1294, 1309 (Fed. Cir. 2010) ("Even if the [patent at issue] were a combination of known elements according to their established functions . . . it yields more than predicable results" and thus is non-obvious.). The district court did not clearly err in determining the scope of Saadah and Raskin. Accordingly, as the district court held, the Saadah reference does not render the '499 and '458 patents obvious to a person of ordinary skill in the art.

iii. *The Henry Ford Patient Records*

Appellants present two patient records from the Henry Ford Clinic in Detroit, Michigan, showing doctors prescribed a daily dose of naproxen as a prophylactic treatment, and sumatriptan for treating acute migraines. Appellants argue that because the two agents would be working in the body at the same time, even if taken separately, they are concomitantly administered. Additionally, Appellants contend that a person of ordinary skill in the art would expect a daily dose of naproxen to have the same effectiveness as a single dose of naproxen taken when needed because concentration of the drug in the blood would be the same or higher. Therefore, Appellants assert that when sumatriptan is taken in addition to a daily dose of naproxen the combination of the two drugs would have the same effect as when the two drugs are given simultaneously.

Dr. Ramadan, who treated the patients at the clinic, testified that he did not recall ever prescribing or giving a patient sumatriptan and naproxen simultaneously. Furthermore, the Henry Ford Records do not suggest that it produced longer lasting efficacy or reduced migraine

relapse. At least one of the patients' prescriptions was soon altered to sumatriptan and an antidepressant, suggesting the combination of sumatriptan and naproxen did not work to relieve migraine symptoms. Accordingly, the district court did not err in its determination of the scope of the teachings of the Henry Ford Records; we hold that the patient records do not render the '499 and '458 patents obvious.

iv. *The Catarci Reference*

The Catarci reference is a case report entitled "Ergotamine-Induced Headache Can Be Sustained By Sumatriptan Daily Intake." Catarci describes a single patient who developed ergotamine-induced headaches and subsequently replaced ergotamine with daily administration of sumatriptan. Sumatriptan effectively alleviated the patient's daily migraines but did not relieve her constant mild headache. Catarci discloses that the patient was subsequently taken off of sumatriptan and NSAIDs were "prescribed both on a daily basis and when required." Catarci discloses that treating the patient's acute migraine attacks with either NSAID or sumatriptan was not beneficial. Instead the patient resumed taking a daily dose of sumatriptan in addition to acupuncture and successfully treated acute migraines with additional sumatriptan. Finally, Catarci concludes that acupuncture is beneficial "in treating drug-induced daily headache." *Pozen*, 800 F. Supp. 2d at 814 (internal citations and quotations omitted).

Appellants argue that Catarci shows a concomitant administration of sumatriptan and naproxen was used to treat migraines as evidenced by the patient's prescription of a daily NSAID as a prophylactic with sumatriptan used as needed.

The district court did not clearly err in finding that Catarci does not teach a combination of sumatriptan and naproxen provided migraine relief. Rather, Catarci concludes that the only effective treatment for this patient was sumatriptan and acupuncture. The district court determined that Catarci discourages combining sumatriptan and naproxen to achieve the claimed efficacy benefits, teaching away from the invention. *Id.*; *see In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994) (A reference teaches away when "a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant."); *see also Spectralytics, Inc. v. Cordis Corp.*, 649 F.3d 1336, 1343 (Fed. Cir. 2011) (explaining that a jury could find that prior art taught away from one solution because all prior art taught a different solution). For the reasons given by the district court, we agree that the Catarci reference does not render the '499 and '458 patents obvious.

v. *Conclusion regarding prior art*

We agree with the district court that the prior art would not have provided one of ordinary skill with motivation to combine sumatriptan and naproxen in order to benefit from longer lasting efficacy as compared to when either agent is taken alone. Appellants failed to rebut the presumption of validity afforded issued patents by clear and convincing evidence. 35 U.S.C. § 282; *Microsoft Corp.*, 131 S. Ct. at 2245; *see Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007) ("[T]he burden falls on the challenger of the patent to show by clear and convincing evidence that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in

doing so."). Therefore, the prior art references do not render the '499 and '458 patents obvious.

2. *The '183 Patent Is Not Invalid For Obviousness*

Par asserts, as it did before the district court, that the '183 patent is obvious in light of the '499 patent, combined with Bandelin and/or knowledge of a person of ordinary skill in the art. Par argues the prior art taught that naproxen has very low solubility in acidic environments like the stomach, which would impede the dissolution of sumatriptan when the two are administered together in a single unit dose. Therefore, a person of ordinary skill in the art would use a multilayer tablet, which was well known, to resolve the physical incompatibility between sumatriptan and naproxen. Additionally, Par contends that the district court failed to apply the correct construction of "independent dissolution" by using the narrow definition in its invalidity analysis when a plain and ordinary definition of the term, which Par argues the district court used to find infringement, would render the claim obvious.

The district court explained that although the references submitted by Par are different than what was before the PTO during prosecution, the content of the references and the arguments made are the same.[9] *Pozen*, 800 F. Supp. 2d at 820. The district court reasoned that, considering the record and the arguments:

> It was not obvious to a person of ordinary skill in the art to formulate the naproxen sodium and sumatriptan into a bilayer configuration. While

[9] The district court considered whether the '183 patent was obvious is light of the '499 patent combined with the Bandelin article that describes how to create and the advantages of multilayer tablets. *Pozen*, 800 F. Supp. 2d at 820.

> multilayer tablets were commonly used, Pozen's dosage forms of naproxen sodium and sumatriptan were not obvious. Nor do the references render obvious the specific tablet architecture as Pozen argued to the PTO and claimed in the '183 patent. Accordingly, Defendants failed to rebut the '183 patent's presumption of validity by clear and convincing evidence.

Id. at 821 (citation omitted). Par concedes that using a "narrow" interpretation of the term "independent dissolution" does not invalidate the '183 patent. We agree.

Par contends that the district court improperly used a different construction of "independent dissolution" in its infringement analysis and invalidity analysis. Par argues that the district court's infringement analysis was conducted under the plain and ordinary meaning of the independent dissolution limitation, whereas the validity analysis uses a narrower definition. *Id.* However, Par fails to explain the "plain and ordinary meaning" of independent dissolution and identify how it differs from the "narrow" meaning. In its infringement analysis the district court construed "independent dissolution" as that term is defined in the '183 patent and does not appear to define that term in its invalidity analysis any differently.[10] Regardless of what definition is applied, Appellants failed to rebut the presumption of validity afforded issued patents by clear and convincing evidence. The district court correctly held that the '183 patent was not obvious.

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[10] *See infra* part C(1).

3. *The '499 Patent Is Not Invalid For Lack Of Written Description*

Appellants argue that the district court erred in finding claim 15 of the '499 patent not invalid because the limitations "therapeutic package," "finished pharmaceutical container," and "said container further containing or comprising labeling directing the use of said package in the treatment of migraine" lack adequate written description in the specification. Appellants assert that the terms were added during prosecution and that, although the exact term need not be recited, "the specification must contain an equivalent description of the claimed subject matter," and there was no description of these limitations. *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 2007).

Section 112, paragraph 1 of the Patent Act, requires that the specification contain a written description of the invention. 35 U.S.C. § 112, ¶ 1. The purpose of the written description requirement is to ensure adequate disclosure of the invention. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). A specification adequately describes an invention when it "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* Following a bench trial, we review compliance with the written description requirement, a question of fact, for clear error. *Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1332 (Fed. Cir. 2008).

The '499 patent discloses several dosage forms, including an oral unit dosage, to teach treating migraines by concomitantly administering therapeutic amounts of sumatriptan and naproxen. '499 patent col.3 ll.22-50, col.4 ll.1-4, col.12 ll.54-55, col.15 ll.12-17. The district court found that "[b]ased on these disclosures, persons of skill

in the art would know these pharmaceutical dosages are administered to a patient in containers or packages with labeling and inserts with dosage instructions." *Pozen*, 800 F. Supp. 2d at 821. Specifically, the district court reasoned that "[d]ispensing pharmaceutical products in containers or packages is not a new or unpredictable concept. A person of ordinary skill in the art would know that medications are not simply handed out to patients. Rather, pharmaceutical products, like the claimed tablets, are routinely administered in containers or packages." *Id.* at 822. Moreover, the FDA requires container labeling and information for prescription pharmaceutical products. *Id.*

The '499 patent specification meets the written description requirement because the specification describes the invention in such a way that it is understandable to a person of ordinary skill in the art. *See Ariad*, 598 F.3d at 1351. As this court has explained, "[i]n order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue . . . . Nonetheless, the disclosure . . . must convey with reasonable clarity to those skilled in the art that . . . [the inventor] was in possession of the invention." *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000); *see LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005) ("[T]he patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before . . . . Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.").

The district court reasonably found that one skilled in the art would understand the meaning of "therapeutic package" and "finished pharmaceutical container." There is no clear error in the district court's finding that there is adequate written description to support the '499 patent validity.

C. The District Court Did Not Err In Finding That Appellants' ANDA Products Infringe The '183 Patent

There are two types of infringement: literal infringement, which is not at issue here, and infringement under the doctrine of equivalents.[11] "The doctrine of equivalents allows the patentee to claim those insubstantial alterations that were not captured in drafting the original patent claim but which could be created through trivial changes." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 733 (2002). "However, the 'all limitations rule' restricts the doctrine of equivalents by preventing its application when doing so would vitiate a claim limitation." *Carnegie Mellon Univ. v. Hoffman-La Roche Inc.*, 541 F.3d 1115, 1129 (Fed. Cir. 2008) (quoting *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 29 (1997)). Equivalence "'is not an absolute to be considered in a vacuum.'" *Warner-Jenkinson*, 520 U.S. at 24-25 (quoting *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 609 (1950)). The essential inquiry is whether "the accused product or process contain[s] elements identical or equivalent to each claimed element of the patented invention." *Id.* at 40. One way of proving infringement under the doctrine of equivalents "is by showing on a limitation by limitation basis that the

[11] To establish literal infringement "every limitation set forth in a claim must be found in an accused product, exactly." *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1575 (Fed. Cir. 1995). The parties do not contest literal infringement in this appeal.

accused product performs substantially the same function in substantially the same way with substantially the same result as each claim limitation of the patented product." *Crown Packaging Tech., Inc. v. Rexam Beverage Can Co.*, 559 F.3d 1308, 1312 (Fed. Cir. 2009). We review the district court's infringement determinations under the doctrine of equivalents for clear error. *Conoco, Inc. v. Energy & Env't Int'l*, 460 F.3d 1349, 1357 (Fed. Cir. 2006).

The district court found that Par and DRL's ANDA products infringed claim 2 of the '183 patent under the doctrine of equivalents. *Pozen*, 800 F. Supp. 2d at 812. On appeal the Appellants challenge the district court's findings that the Appellants' ANDA products meet the "independent dissolution" limitation and the "substantially all" limitation. We address each in turn.

1. *The "Independent Dissolution" Limitation*

The parties agreed that the limitation "dissolution of said naproxen occurs independently of said triptan" as recited in claim 1 of the '183 patent means "[d]issolution of naproxen . . . and triptan from the multilayer tablet . . . occurs in the same amount of time ± 10% as when the same amount of naproxen . . . and triptan are given separately" as it was described in the patent specification. J.A.653; '183 patent col.2 ll.48-54. Based on the evidence presented the district court found "Pozen has shown by a preponderance of the evidence the accused ANDA products achieve independent dissolution." *Pozen*, 800 F. Supp. 2d at 811-12.

Relying upon Par's FDA filings and expert testimony presented at trial, the district court found that Par's ANDA product performs the same function in the same way to achieve the same results and therefore satisfies the independent dissolution limitation under the doctrine of equivalents. *Pozen*, 800 F. Supp. 2d at 810. Pozen's

expert noted that Par's ANDA product was specifically formulated to achieve complete and independent dissolution. J.A.6029. Moreover, in its ANDA, Par represented to the FDA that the sumatriptan and naproxen in its ANDA product dissolves completely and independently from each other. J.A.157587; J.A.157602; J.A.158055.[12]

The district court similarly found that DRL's ANDA product achieves independent dissolution "by the way it formulates and manufactures the tablets." *Pozen*, 800 F. Supp. 2d at 810. Relying upon the parties' ANDA disclosures and expert testimony, the district court found that "substantially all the triptan is segregated and separated into the equivalent of a first distinct layer, in an equivalent side-by-side arrangement, and this achieves the result of independent dissolution." *Id.* at 811. Moreover, the district court found "DRL's testing of its ANDA product confirms its independent dissolution." *Id.*[13]

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[12] Par's ANDA states:

> Most of our experiments were targeted to match the in-vitro dissolution profile of the individual brands. Naproxen Sodium, is poorly soluble in lower pH conditions, and tends to form a gel like matrix and thereby retard the release of co-administered drugs. Our primary objective is to develop a formulation having minimal effect of Naproxen Sodium over Sumatriptan Succinate dissolution, thereby having release profiles independent of each other in all the pH conditions. . . .

J.A.157602.

[13] Comparing DRL's dissolution profile of its ANDA product to Table 7 in the '183 patent, which shows the dissolution profile of sumatriptan in a bilayer tablet, Pozen's expert, Dr. Williams, opined that the dissolution results in the table were almost the same as those in DRL's ANDA product. J.A.6063-64.

Notwithstanding the evidence presented at trial, Appellants argue that Pozen did not prove independent dissolution because there is no evidence on the record that the comparison required by the '183 patent was ever undertaken. Specifically, Appellants contend that there is no proof that the independent dissolution achieved by the ANDA products was compared to dissolution rates of the same amount of naproxen or sumatriptan alone. Appellants thus ask this court to find the district court erred by not requiring any proof that the active agents in their ANDA products achieved dissolution in about the same time (± 10%) it would take for either of the active agents to achieve dissolution when taken alone.

The district court did not clearly err in finding infringement under the doctrine of equivalents because the record contains sufficient evidence that the independent dissolution requirement of the '183 patent was met. In assessing equivalents, the court considers whether "the accused product[s] perform[] substantially the same function in substantially the same way with substantially the same result as each claim limitation of the patented product." *Crown Packaging Tech.*, 559 F.3d at 1312. Although there is no direct evidence comparing the rate of dissolution of the ANDA products to that of the agents individually, no such actual comparison was necessary. Under the doctrine of equivalents analysis Pozen need only show that the ANDA products performed the same function in the same way to achieve the same result as the claimed elements of the '183 patent. Par and DRL provided expert testimony to show that the sumatriptan dissolves completely and independently from the naproxen and that the naproxen dissolves completely and independently from the sumatriptan in their ANDA products. Also, there is probative evidence from Par's ANDA and comparison of DRL's ANDA products dissolu-

tion profile showing that their sumatriptan and naproxen dissolve completely and independently from another. As a result, Appellants offer no basis for setting aside the district court's finding. Indeed, there is sufficient evidence showing that logically if the agents dissolve in the same way they would if the other agent was not present, their dissolution takes the same amount of time it would taken when given separately. Thus, the district court did not clearly err in relying on Pozen's expert testimony and concluding that Appellants' ANDA products meet the "independent dissolution" limitation as recited in claim 1 of the '183 patent under the doctrine of equivalents.

2. *Infringement Of The "Substantially All" Limitation*

Claim 1 of the '183 patent requires "substantially all of said triptan is in the first layer of said tablet and substantially all of said naproxen is in a second, separate layer." '183 patent col.18 ll.30-39. The district court construed this phrase as "at least 90%, and preferably greater than 95%, of the total triptan present in the tablet is included within one distinct layer and at least 90%, and preferably greater than 95%, of the naproxen present in the tablet is included within a second distinct layer." *Pozen Inc. v. Par Pharm., Inc.*, 719 F. Supp. 2d 718, 734 (E.D. Tex. 2010). It is undisputed that the first layer of Par's ANDA tablet "contains 100% of the tablet's sumatriptan, along with 15% of the tablet's naproxen, with the remaining 85% of the naproxen in the second layer. DRL's ANDA tablet has 100% of the tablet's naproxen and 15% of the tablet's sumatriptan in the first layer, with the remaining 85% of the sumatriptan in the second layer." *Pozen*, 800 F. Supp. 2d at 809.

i. *The doctrine of equivalents can apply to the "substantially all" limitation*

The district court recognized that the claim construction of the term "substantially all" provided specific percentages but stated that "absent more limiting language in the intrinsic record" the doctrine of equivalents can be applied to find infringement where the accused value is insubstantially different from the claimed value. *Id.* (quoting *Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1292 (Fed. Cir. 2010)); *see also U.S. Philips Corp. v. Iwasaki Elec. Co.*, 505 F.3d 1371, 1378 (Fed. Cir. 2007) (holding that despite a claimed concentration range the doctrine of equivalents can still be applied).

Par argues that the district court improperly treated the claim term "substantially all" as a precise quantity entitled to the doctrine of equivalents when it is really a "fuzzy" quantitative limitation not entitled to equivalents. Par asserts that the word "substantially" was used to capture values lower than 100%, indeed the district court construed the term to include any amount as low as 90%, and Par contends Pozen should not reach below 90% "to encompass equivalents of equivalents." *Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1372 (Fed. Cir. 2008).

DRL argues that the district court erred in granting Pozen a range of equivalency for the '183 patent beyond the scope of equivalency determined through claim construction. DRL asserts that in the cases the district court cites the degree to which the accused product fell outside the specifically claimed range was miniscule in comparison to the amount their ANDA product falls outside of the claimed range.[14] Here, DRL contends, sumatriptan only

[14] In *Adams Respiratory* the requirement was "at least 3500 units" and the accused product had 3493.38

makes up 85% of one layer; 5% less than the minimum 90% set forth in the construction of the term "substantially all."

Indeed, this court has stated that where "a patentee has brought what would otherwise be equivalents of a limitation into the literal scope of the claim, the doctrine of equivalents is unavailable to further broaden the scope of the claim." *Cohesive Techs.*, 543 F.3d at 1372. "[A]ll claim limitations are not entitled to an equal scope of equivalents. Whether the result of the All Limitations Rule, prosecution history estoppel, or the inherent narrowness of the claim language, many limitations warrant little, if any, range of equivalents." *Moore U.S.A., Inc. v. Standard Register Co.*, 229 F.3d 1091, 1106 (Fed. Cir. 2000) (internal citations omitted).

However, although the claim language itself is a qualitative measure, the claim construction pulls directly from the specification to give the term "substantially all" a quantitative definition, specifically, "at least 90%, and preferably greater than 95%," '183 patent col.2 ll.62-65, and this court has previously concluded that the doctrine of equivalents is not foreclosed with respect to claimed ranges, *see Adams Respiratory*, 616 F.3d at 1291-92. In *Kemin Foods*, the court construed "substantially free from other carotenoids" to mean "significantly less than 10% of other carotenoids" based, in part, on the specification stating that "[g]enerally, the concentration of other carotenoids in the starting material should be 10% or less." *Kemin Foods, L.C. v. Pigmentos Vegetales Del Centro S.A.*

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units, within 0.189% of the claimed minimum. *Adams Respiratory*, 616 F.3d at 1291. In *Abbott Laboratories*, the claim required between 68.8% and 94.5% by weight of a component, and the accused product had 95% of that component. *Abbott Laboratories v. Dey L.P.*, 287 F.3d 1097, 1107 (Fed. Cir. 2002).

de C.V., 464 F.3d 1339, 1349 (Fed. Cir. 2006). The court determined that because Kemin did not argue that "significantly less than 10%" has a precise upper limit a reasonable person could determine that a concentration of 6.14%-9.86% does not infringe under the doctrine of equivalents. *Id.* Similarly, in this case, Pozen never stated that "at least 90%, and preferably greater than 95%" should be an absolute floor. Under the doctrine of equivalents a tablet layer with 85% of the agent can be fairly characterized as an insubstantial change from a tablet layer with 90% of the agent.

ii. *Appellants' ANDA products infringe the "substantially all" limitation under the doctrine of equivalents*

Turning now to the district court's analysis of infringement of the "substantially all" limitation, we review the district court's findings of infringement under the doctrine of equivalents for clear error. *Conoco*, 460 F.3d at 1357. The district court stated that the multilayer tablet claimed in the '183 patent requires "substantially all of the naproxen and triptan [to be] segregated and separated for the purpose of independent dissolution." *Pozen*, 800 F. Supp. 2d at 810. The parties' experts agreed that the function was to have "separate, distinct layers of sumatriptan and naproxen. The way in which this function is achieved is by formulating the sumatriptan and naproxen in different manners to create physical barriers. The result is that substantially naproxen is separated from the [sumatriptan], thereby providing independent dissolution." *Id.*

The district court found that Par's ANDA product performs essentially the same function, by segregating the naproxen and sumatriptan into two layers. *Id.* This is achieved by formulating them differently, specifically, by

using a polymer binder to form 15% of the naproxen into granules which are added to the sumatriptan layer. *Id.* The result is that one layer has 100% of the sumatriptan with 15% of the naproxen, and another layer has the remaining 85% of the naproxen, substantially all separated and segregated into two layers. *Id.* Therefore, the district court determined, Par's ANDA product performs the same function, in the same way, and achieves the same result, and satisfies all of the limitations of the '183 patent under the doctrine of equivalents.

The district court also found that DRL's ANDA product performs the same function of achieving separate, distinct layers by segregating the triptan and naproxen. *Id.* This is achieved by granulating 15% of the sumatriptan with a polymer binder and then spraying it on the naproxen which has been granulated with a polymer binder as well; the remaining 85% of the sumatriptan forms the other layer. *Id.* "Thus, substantially all the triptan is segregated and separated into the equivalent of a first distinct layer, in an equivalent side-by-side arrangement, and this achieves the result of independent dissolution." *Id.* at 811. Therefore, the district court determined, DRL's ANDA product performs the same function, in the same way, and achieves the same result, and satisfies all of the limitations of the '183 patent under the doctrine of equivalents.

Appellants argue that their ANDA products do not achieve separate distinct layers because one of the layers has both agents. However, their products contain a bilayer tablet, with 100% of one agent in one layer, and 85% of the other agent in the other layer. We determine, as the district court did, that this structure is insubstantially different from a bilayer tablet with 90% of the total therapeutic agent present in the tablet included in a single layer.

Appellants contend that their products are admixtures which Pozen specifically disclaimed during the '183 patent prosecution. DRL argues that the district court improperly limited Pozen's disclaimer to admixtures that achieve independent dissolution, when it really disclaimed admixtures in general. We agree that Pozen did in fact disclaim admixtures when it stated before the PTO:

> The present claims require that naproxen and [sumatriptan] be in a tablet in which they are segregated from one another in a "side by side arrangement" and in which their dissolution occurs independently of one another. The claims are limited to one very specific tablet architecture. Among the dosage forms falling outside the claims are: admixtures; any dosage forms other than tablets; tablets in which one drug is in a core and surrounded by a layer or coating containing the second drug; and tablets containing multiple drug release pellets or microparticles.

J.A.240667. However, the Appellants' ANDA products are not admixtures, i.e. substances with blended or mixed ingredients, because substantially all of the agents are separated and segregated into two distinct layers, as explained above.

Based on the evidence above, the district court did not clearly err in finding that Par's ANDA products and DRL's ANDA products met the "substantially all" limitation of the '183 patent under the doctrine of equivalents.

CONCLUSION

Appellants failed to rebut the presumption of validity of issued patents, thus, we affirm the district court's holding that the '499, '458, and '183 patents are not

invalid. Additionally the Appellants provided no basis for unsettling the district court's finding on infringement. Accordingly, we affirm the district court's injunction enjoining Appellants from making, using, importing, selling or offering to sell their ANDA products, or inducing others to do so, until the expiration of the '499, '458, and '183 patents.

AFFIRMED

United States Court of Appeals for the Federal Circuit

POZEN INC.,
Plaintiff-Appellee,

v.

PAR PHARMACEUTICAL, INC.,
Defendant-Appellant,

AND

DR. REDDY'S LABORATORIES, INC.,
Defendant-Appellant,

AND

ALPHAPHARM PTY LTD.,
Defendant-Appellant.

2011-1584, -1585, -1586

Appeal from the United States District Court for the Eastern District of Texas in Consolidated Case Nos. 08-CV-0437, 09-CV-0003, and 09-CV-0182, Judge Leonard Davis.

CLEVENGER, *Circuit Judge*, dissenting-in-part.

I join the court's opinion in all respects but one. The District Court erred in finding infringement of claim 2 of the '183 patent under the doctrine of equivalents, and the

court today errs in sustaining the judgment of the District Court on this issue.

Claim 2 calls for a multilayer pharmaceutical tablet comprising naproxen and a triptan wherein "substantially all of said triptan is in a first layer of said tablet and substantially all of said naproxen is in a second, separate layer." This claim language begged the question of how much by volume of both naproxen and triptan less than 100% is "substantially all." The District Court answered the question, construing "substantially all" without objection to mean:

> "[A]t least 90%, and preferably greater than 95%, of the total triptan
>
> present in the tablet is included within one distinct layer and at least
>
> 90%, and preferably greater than 95%, of the naproxen present in
>
> the tablet is included within a second distinct layer."

The accused products do not literally meet the "substantially all" limitation. That is why the patentee could not assert literal infringement of claim 2, and why he was forced to rely on the doctrine of equivalents to establish infringement. The actual composition of the claimed and accused tablets, with regard to the "substantially all" limitation, is shown on the following chart.

	Claimed Product	Par's ANDA product	DRL's ANDA product
Layer 1	≥90% total amt. of sumatriptan, ≤10% total amt. of naproxen	~100% total amt. of sumatriptan, ~15% total amt. of naproxen (granules)	~85% total amt. of sumatriptan
Layer 2	≥90% total amt. of naproxen, ≤10% total amt. of sumatriptan	~85% total amt. of naproxen	~100% total amt. of naproxen (granules), ~15% total amt. of sumatriptan (sprayed on granules)

As shown in the table above, each of the Par and DRL products includes one more or less "pure" layer meeting the "substantially all" limitation as defined by the District Court. Par's product has substantially all the required triptan in one layer along with 15% of the tablet's naproxen, but the second Par layer has less than 90% of naproxen. So the question is whether 85% of naproxen is equivalent to 90%, when "substantially all" means "at least 90% and preferably greater than 95%.

DRL's product is also designed to avoid the "substantially all" limitation. It has substantially all the required naproxen in one layer, along with 15% of the triptan, but the second DRL layer has only 85% of the total triptan in the product. So, again, the question is whether 85% can be "substantially all" given the District Court's construction of the limitation.

Pozen candidly admits in its brief to this court that the District Court never directly addressed the question of whether a layer containing 85% of a necessary ingredient is an equivalent of a layer containing at least 90% and preferably 95% of the necessary ingredient. And Pozen says it does not argue that 85% can be a numerical equivalent of 90%. Instead, Pozen argues that the District Court properly elided the numeric equivalence issue by asking only if the accused products had an "equivalent of a second layer" which could be viewed as containing substantially all of the required ingredient. Pozen and the District Court both see the "substantially all" limitation as requiring the tablet to have one more or less pure layer, and not an actual second layer but an "equivalent" second layer that could be said to be equivalent to a more or less pure layer even if it failed to contain substantially all of the required ingredient. In short, Pozen and the District Court used the notion of an equivalent layer simply to avoid answering the question of whether 85% is the equivalent of 90% or preferably 95%.

Even if the equivalent layer notion has merit, it still cannot be disconnected from the language of the claim. The equivalent layer would, in any event, have to be the equivalent of a more or less pure layer, i.e., one with at least 90% and preferably 95% of the required ingredient in it. How can a layer with only 85% of the necessary ingredient in it be an equivalent of a layer with at least 90% and preferably 95% of the required ingredient in it?

The District Court, with no contest from Pozen, recognized that "substantially all" inherently contains a range from something less than 100% up to 100%. Rather than leave the inherent equivalent range embedded in the claim language, the District Court put boundaries on the claim language. "Substantially all" means at least 90% and preferably 95%. The defendants cite our precedent, including *Moore U.S.A., Inc. v. Standard Register Co.*, 229 F.3d 1091 (Fed. Cir. 2000), for the proposition that the spread from 85% to 90% is too great to be an equivalent. Pozen appreciates the force of those cases, but argues they are inapplicable here because the District Court did not answer the numeric equivalence question but instead turned the infringement decision on a flawed layer equivalence notion.

In my view, the District Court erred by not asking itself if under claim 2 a layer, viewed from the outside or from the inside, can be equivalent if is numerically non-equivalent. It cannot. The majority states that "a reasonable person could determine that a tablet layer with 85% of the agent is within the scope of the doctrine of equivalents." Respectfully, I disagree.