UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

WARNER-LAMBERT COMPANY,	)	
Plaintiff,	)	
v.	)	Civil Action No. 99-922 (DRD)
TEVA PHARMACEUTICALS USA, INC.,	)	Hon. Dickinson R. Debevoise
Defendant.	)	

POST-TRIAL BRIEF OF TEVA PHARMACEUTICALS USA, INC.

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TABLE OF CONTENTS

TABLE OF AUTHORITIES v

TABLE OF ABBREVIATIONS ix

INTRODUCTION 1

STATUS OF THE CASE 4

ARGUMENT 5

I. The '450 Patent is Unenforceable Due to Warner-Lambert's Inequitable Conduct Before the PTO. 5

A. Warner-Lambert Inventors Were Thoroughly Acquainted With Merck's Enalapril Product And Filed a Patent Application that Encompassed It. 6

1. Warner-Lambert Extensively Monitored Merck's Enalapril Product Prior to its Launch as Vasotec in the U.S. in January 1986. 6

2. Warner-Lambert Continued to Analyze Vasotec After Vasotec's U.S. Launch in January 1986. 9

3. The Development of Quinapril Culminated in the Filing of an Overreaching Patent Application that Encompassed Vasotec. 16

B. Warner-Lambert Intentionally Failed to Inform the PTO About Vasotec — Which Was "Highly Material" Prior Art — and Therefore Committed Inequitable Conduct that Renders the '450 Patent Unenforceable. 19

1. The Higher the Level of the Materiality of the Withheld Information, the Lower the Level of Intent Required. 20

2. As This Court Has Already Found, Vasotec Was Highly Material Prior Art. 20

3. The Inventors of the '450 Patent Intentionally Withheld Vasotec From the PTO. 21

a. The Inventors of the '450 Patent Knew that the '450 Patent Application Read on Vasotec and that Vasotec was Material. 22

b. The Inventors of the '450 Patent Deliberately Chose to Hide the Existence of Vasotec From Their Patent Attorney and the PTO. 25

4. Warner-Lambert Offers No Plausible Justification For the Conduct of the Inventors of the '450 Patent. 32

a. "Sodium Bicarbonate Fell Off the Table" is No Excuse. 33

b. "In [Dr. Murthy's] View Bohidar Was Not Prior Art" is No Excuse 35

c. "Patent Attorneys By Nature Try and Claim the World" is No Excuse 36

5. Dr. Murthy's Evasiveness Confirms the Inventors' Intent to Deceive. 38

6. A Finding of Unenforceability is Appropriate. 45

II. Claims 16 and 17 of the '450 Patent Are Invalid. 47

A. Claims 16 and 17 are Anticipated by Merck's Prior Practice of the Vasotec Process. 48

1. Patents That Claim Inventions in the Prior Art are Invalid. 48

2. The Claimed Invention Was Made by Merck's Prior Art Vasotec Process. 49

3. The Vasotec Process Qualifies as Prior Art Because it Occurred in the United States Prior to the Invention Date of the Claims of the '450 Patent. 52

4. Merck Did Not Abandon, Suppress, or Conceal the Vasotec Process 53

a. Six Merck-Related References Disclose Every Limitation of Claims 16 and 17 of the '450 Patent..... 54

b. All Six Merck References Should be Considered to Demonstrate that Merck Did Not Abandon, Suppress, or Conceal the Vasotec Process..... 58

c. Dr. Brenner's Testimony Does Not Negate a Finding that Merck Did Not Abandon, Suppress, or Conceal the Vasotec Process. 59

B. Claims 16 and 17 Are Invalid Because They Are Obvious in View of the Prior Art 62

1. The Prior Art Includes *Dictionnaire Vidal*, *Pharmaceutisch Weekblad*, Kato, the Vasotec Package Insert, Bohidar et al., and Shiromani et al 63

2. The Prior Art Expressly Urges Persons Skilled in the Art to Make and Use the Combination That Warner-Lambert Later Claimed as an Invention 64

3. A Person of Ordinary Skill in the Art Would Have Had Access to All Cited Prior Art References 68

4. No Evidence of Secondary Considerations Can Overcome the Explicit Teaching of the Prior Art 70

CONCLUSION 73

TABLE OF AUTHORITIES

Cases

A.B. Dick Co. v. Burroughs Corp., 798 F.2d 1392 (Fed. Cir. 1986) 21

Apotex v. Merck, 253 F.3d 1031 (Fed. Cir. 2001) 61

Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342 (Fed. Cir. 1999) 48

Brasseler, U.S.A. v. Stryker Sales Corp., 267 F.3d 1370 (Fed. Cir. 2001) 32, 43, 44

Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., 326 F.3d 1226 (Fed. Cir. 2003) 32

Brown & Williamson Tobacco Corp. v. Philip Morris Inc., 229 F.3d. 1120 (Fed. Cir. 2000) 70

Checkpoint Sys. v. United States Int'l Trade Comm'n, 54 F.3d 756 (Fed. Cir. 1993) 60

Cooper Cameron Corp. v. Kvaerner Oilfield Prods., 291 F.3d 1317 (Fed. Cir. 2002) 64

Critikon, Inc. v. Becton Dickinson Vascular Access, Inc., 120 F.3d 1253 (Fed. Cir. 1997) 20, 22, 25, 38

Dow Chem. v. Astro-Valcour, Inc., 267 F.3d 1334 (Fed. Cir. 2001). 49, 53

E.I. DuPont de Nemours & Co. v. Phillips Petroleum Co., 849 F.2d 1430 (Fed. Cir. 1988) 60

Elk Corp. of Dallas v. GAF Bldg. Materials Corp., 168 F.3d 28 (Fed. Cir. 1999) 20

FMC Corp. v. Hennessy Indus., 836 F.2d 521 (Fed. Cir. 1987). 32

FMC Corp. v. Manitowoc Co., 835 F.2d 1411 (Fed. Cir. 1987) 37

Fox Indus. v. Structural Preservation Sys., 922 F.2d 801 (Fed. Cir. 1990) 5, 6

Frazier v. Roessel Cine Photo Tech., 2003 US Dist. LEXIS 19607 (C.D. Cal. Apr. 9, 2003) 29, 35, 36

Gardco Mfg., Inc. v. Herst Lighting Co., 820 F.2d 1209 (Fed. Cir. 1987) 21

GFI, Inc. v. Franklin Corp., 265 F.3d 1268 (Fed. Cir. 2001) 31

GFI, Inc. v. Franklin Corp., 88 F. Supp. 2d 619 (N.D. Miss. 2000) 38, 47

Graham v. John Deere Co., 383 U.S. 1 (1966) ..... *passim*

In re Cruciferous Sprout Litigation, 301 F.3d 1343 (Fed. Cir. 2002) 48

In re GPAC Inc., 57 F.3d 1573 (Fed. Cir. 1995) 63, 72

In re Huang, 100 F.3d 135 (Fed. Cir. 1996) 62

In re Larson, 340 F.2d 965 (C.C.P.A. 1965) 63

In re Rouffet, 149 F.3d 1350 (Fed. Cir. 1998) 69

Innovative Scuba Concepts, Inc. v. Feder Industries, Inc., 26 F.3d 1112 (Fed. Cir. 1994) 58

ISCO Int'l, Inc. v. Conductus, Inc., 279 F. Supp. 2d 489 (D. Del. 2003) 47

Kearns v. Ford Motor Co., 114 F.R.D. 57 (E.D. Mich. 1987) 44

Key Pharms. v. Hercon Labs. Corp., 161 F.3d 709 (Fed. Cir. 1998) 38

Li Second Family Ltd. P'ship v. Toshiba Corp., 231 F.3d 1373 (Fed. Cir. 2000) 5, 21

Liquid Carbonic Corp. v. Goodyear Tire & Rubber Co., 38 F. Supp. 520 (N.D. Ohio 1941) 46

Mahurkar v. C.R. Bard Inc., 79 F.3d 1572 (Fed. Cir. 1996) 58

McNeil-PPC, Inc. v. L. Perrigo Co., 337 F.3d 1362 (Fed. Cir. 2003) 70

Merck & Co. v. Biocraft Labs., 874 F.2d 804 (Fed. Cir. 1989). 62, 63

Minton v. Nat'l Assoc. of Securities Dealers, Inc., 226 F. Supp. 2d 845 (E.D. Tex. 2002) 69

Molins PLC v. Textron, Inc., 48 F.3d 1172 (Fed. Cir. 1995) 5, 29

Novo Nordisk A/S v. Becton Dickinson & Co., 304 F.3d 1216 (Fed. Cir. 2002) 69

Oak Indus. v. Zenith Elecs., 726 F. Supp. 1525 (N.D. Ill. 1989) 60

Paragon Podiatry Lab. v. KLM Lab., 984 F.2d 1182 (Fed. Cir. 1993) 22

Paulik v. Rizkalla, 760 F.2d 1270 (Fed. Cir. 1985). 58

Precision Instrument Mfg. v. Auto. Maint. Mach., 324 U.S. 806 (1945) 5

Sadler-Cisar, Inc. v. Commercial Sales Network, Inc., 786 F. Supp. 1287 (N.D. Ohio 1991) 46

Semiconductor Energy Lab. v. Samsung Elecs., 204 F.3d 1368 (Fed. Cir. 2000) 22

Semiconductor Energy Lab. v. Samsung Elecs., 4 F. Supp. 2d 477 (E.D. Va. 1998) 44

SIBIA Neurosciences, Inc. v. Cadus Pharm. Corp., 225 F.3d 1349 (Fed. Cir. 2000) 65

Slip Track Sys. v. Metal-Lite, Inc., 304 F.3d 1256 (Fed. Cir. 2002) 59

Titanium Metals Corp. of America v. Banner, 778 F.2d 775 (Fed. Cir. 1985). 48

Woodland Trust v. Flowertree Nursery, Inc., 148 F.3d 1368 (Fed. Cir. 1998) 58, 59

Statutes

35 U.S.C. § 102 ..... *passim*

35 U.S.C. § 103 ..... *passim*

35 U.S.C. § 112 61

35 U.S.C. § 115 45

TABLE OF ABBREVIATIONS

Accupril	Accupril®, Warner-Lambert's commercial quinapril hydrochloride product
ACE	Angiotensin-converting enzyme
ANDA	Abbreviated New Drug Application
Bohidar et al.	Bohidar, Bavitz and Shiromani, *Formula Optimization for a Multiple Potency System with Uniform Tablet Weight*, 12(10) *Drug Dev. & Indus. Pharmacy* 1503-10 (1986)
Cl. Const. Order	June 13, 2002, Claim Construction Order of Judge Debevoise
Cl. Const. Stip.	May 7, 2003, Stipulation and Order regarding certain claim terms of the '450 patent
Dictionnaire Vidal	*Dictionnaire Vidal* 10 (1985)
DTX	Defendant's Trial Exhibit
FDA	U.S. Food and Drug Administration
Fed. Cir. Op.	January 29, 2004, Opinion of the Federal Circuit in *Schwarz Pharma v. Teva*
Kato	Toshihiro Kato, *Flow-Injection Spectrophotometric Determination of Enalapril in Pharmaceuticals with Bromothymol Blue* in 175 *Analytica Chimica Acta* 339 (1985)
Koch	*Enalapril: New Antihypertensive of the ACE-Inhibitors type,* in 6 *Pharmacy International* 287 (1985)
Merck	Merck & Co., Inc.

NDA	New Drug Application
Orange Book	FDA publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations"
Pharmaceutisch Weekblad	*Enalapril (Renitec), Famacotherapeutische Egevens*, 120(39) *Pharmaceutisch Weekblad* 799-800 (1985)
'pril	Class of ACE inhibitor drugs used to treat high blood pressure
PTO	U.S. Patent and Trademark Office
PTX	Plaintiff's Trial Exhibit
Shiromani et al.	Shiromani and Bavitz, *Effect of Moisture on the Physical and Chemical Stability of Granulations and Tablets of the Angiotensin Converting Enzyme Inhibitor, Enalapril Maleate,* 12(14) *Drug Dev. & Indus. Pharmacy* 2467-80 (1986)
S.J. Op.	October 2, 2003, Summary Judgment Opinion of Judge Debevoise
Squibb	Squibb Institute for Medical Research
Teva	Teva Pharmaceuticals USA, Inc.
the '450 patent	U.S. Patent No. 4,743,450, the patent in suit
Vasotec	Vasotec®, Merck's commercial product made using at least the starting ingredients of enalapril maleate, sodium bicarbonate and lactose
Vasotec Process	The process of manufacturing the Vasotec tablets for commercial sale using at least the starting ingredients of enalapril maleate, sodium bicarbonate, and lactose

Warner-Lambert	Warner-Lambert Company

INTRODUCTION

When the Warner-Lambert scientists filed the '450 patent in 1987, they knew that Merck's Vasotec product consisted of an "ACE inhibitor" (enalapril) that was stabilized against cyclization by mixing it with an "alkali metal salt" (sodium bicarbonate) and a "saccharide" (lactose), exactly as they claimed to have invented. They would have this Court believe that their failure to disclose Vasotec to the Patent Office was innocent, notwithstanding this knowledge. But their uncorroborated protestations of innocence cannot be squared with the evidence presented at trial. The only plausible conclusion is that they deliberately suppressed highly material prior art because it threatened the patent they sought for Warner-Lambert. Their inequitable conduct renders the patent unenforceable.

Warner-Lambert's tortured efforts to avoid the finding that their scientists intended to deceive the Patent Office by suppressing prior art that was not only highly material, as this Court has already found, but actually invalidating, do not pass the "blush test." Drs. Harris and Murthy assert that "sodium bicarbonate" did not "work" to stabilize Warner-Lambert's drug, quinapril. Ignore, for the moment, the documents that make it clear that the inventors considered sodium bicarbonate a potential stabilizer well after the experiments that purportedly showed that sodium bicarbonate "did not work." Whatever their experience with quinapril, the

inventors knew that sodium bicarbonate did stabilize the enalapril in Vasotec and that their claims covered enalapril stabilized with sodium bicarbonate.

Dr. Murthy, who consistently tried to evade any questions about the undeniable fact that the claims of the '450 patent encompassed Vasotec, also tried to slough any blame for his attempt to claim Merck's invention onto his lawyers by characterizing patent lawyers as invariably and incorrigibly trying to "claim the world." It is a sign of Warner-Lambert's desperation that it was reduced to such a defense. If Dr. Murthy genuinely believed his lawyer would draft overbroad claims, then he had even less excuse, after reading the patent application carefully, not to tell the patent lawyer that the application claimed someone else's earlier invention. *A fortiori*, Dr. Murthy and his fellow inventors, cognizant of their legal obligations to the Patent Office, could not have failed to disclose Vasotec at all — however tolerant they might have been of aggressive claim drafting — were they not determined to keep that prior art hidden from the examiner.

In addition, claims 16 and 17 of the '450 patent are invalid. First, they are anticipated by Vasotec under 35 U.S.C. § 102(g)(2). Warner-Lambert tries to obscure the anticipation issue by focusing on the extent to which Merck preserved as a trade secret the "know-how" needed to manufacture Vasotec. Even if this were true, it is beside the point because this "know-how" has no bearing on the actual inventions that were claimed by Warner-Lambert. Teva proved by clear and

convincing evidence that Warner-Lambert's ***claimed invention*** was first made by Merck and Merck did not abandon, suppress or conceal ***this invention***. Under § 102(g)(2), claims 16 and 17 are anticipated.

Moreover, claims 16 and 17 are invalid as obvious under 35 U.S.C. § 103. The undisputed testimony established that Vasotec embodies the claimed process. Moreover, Merck published sufficient information before the invention date — whatever that date may be found to be — to make this embodiment obvious to a person of ordinary skill in the art, just as Dr. Murthy himself correctly discerned.

That Accupril may have enjoyed a degree of commercial success is irrelevant to the analysis because the undisputed evidence, including testimony by the only Warner-Lambert witnesses to address the issue, is that the inventions claimed in the '450 patent had nothing to do with that success. All these inventions did was permit satisfaction of FDA stability requirements. But that is true for any other ACE inhibitor that doctors might prescribe for hypertension. Since the '450 patent gave no competitive advantage, there was no nexus between the invention and Accupril's commercial success.

STATUS OF THE CASE

During a four-day trial from May 3-6, 2004, the following issues were tried before the Court:[1]

- Whether Dr. Murthy and the other named inventors intended to deceive the Patent Office, thereby rendering the '450 patent unenforceable because of inequitable conduct, when they failed to inform the PTO about Vasotec despite: (i) extensive and multi-faceted knowledge concerning the stabilization of Vasotec; and (ii) the fact that the patent application embraced Vasotec.

- Whether claims 16 and 17 of the '450 patent are invalid: (i) because they encompass the prior art process of stabilizing Vasotec, which was developed and performed by Merck and made publicly available through several Merck publications; or (ii) because those claims were obvious in light of the prior art.

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[1] After several years of discovery, both parties filed summary judgment motions in the summer of 2003. In ruling on these motions, the Court issued the following findings (among others) on October 2, 2003:

- Teva's quinapril hydrochloride formulation proposed in its ANDA infringes claims 1, 4-10, 12, 16, and 17 of the '450 patent, S.J. Op., at 55;

- Claims 1, 4-10, and 12 of the '450 patent are not invalid, S.J. Op., at 55; and

- The existence of Merck's Vasotec formulation was "highly material" information with respect to the prosecution of the application that led to the '450 patent, S.J. Op., at 49, 51.

ARGUMENT

I. The '450 Patent is Unenforceable Due to Warner-Lambert's Inequitable Conduct Before the PTO.

Patent prosecution is by its very nature *ex parte*. The applicant and the examiner engage in a confidential negotiation, sometimes extending over a period of years, to define the rights of the inventors. Although the rights of both competitors and the public are directly implicated in the patent application process, they may not participate in that process to prevent overreaching by the applicant. Accordingly, patent law imposes on the applicant a very strict duty of "candor, good faith, and honesty." *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1178 (Fed. Cir. 1995) (citing *Precision Instrument Mfg. v. Auto. Maint. Mach.*, 324 U.S. 806, 818 (1945)). The applicant must call to the attention of the PTO ***any*** information material to the application, of which the inventor is aware, whether or not it would ultimately preclude issuance of the patent. *Li Second Family Ltd. P'ship v. Toshiba Corp.*, 231 F.3d 1373, 1380-81 (Fed. Cir. 2000). "A breach of this duty constitutes inequitable conduct." *Molins*, 48 F.3d at 1178.

The duty of candor is not limited to claims that are ultimately allowed following prosecution. On the contrary, a breach of the duty of candor at any point in the prosecution of the application may constitute inequitable conduct. *Fox Indus. v. Structural Preservation Sys.*, 922 F.2d 801, 803-04 (Fed. Cir. 1990).

The penalty for a deliberate failure to disclose material information is appropriately severe — the patent in question is rendered unenforceable. *Id.* at 804. The penalty of unenforceability is warranted in this case.

A. Warner-Lambert Inventors Were Thoroughly Acquainted With Merck's Enalapril Product and Filed a Patent Application that Encompassed It.

At each step of the development of quinapril, Warner-Lambert scientists used Merck's enalapril product as a point of reference and comparison — except at the critical time when their obligation was to disclose information material to the prosecution of their patent application.

1. Warner-Lambert Extensively Monitored Merck's Enalapril Product Prior to its Launch as Vasotec in the U.S. in January 1986.

In the early 1980s, captopril, Squibb's first-generation ACE-inhibitor product, was the only ACE-inhibitor on the market. The demand for anti-hypertensive products drove Warner-Lambert and other pharmaceutical companies to race to develop a second-generation 'pril. Murthy 365:15-366:6. Beginning in 1981, scientists at Warner-Lambert, including Dr. Kuchi S. Murthy, met regularly to develop such a product based on quinapril. Murthy 366:7-367:16. At about the same time, Merck — a competitor of Warner-Lambert — was also developing a product containing its own ACE inhibitor compound, enalapril. DTX 301, at A1107 ¶ 5.

From 1981 to 1985, Warner-Lambert used enalapril as a reference and point of comparison for a variety of decisions about quinapril, including its pharmacology, nomenclature, chemical analysis, dosage size, financial projections, licensing strategy, and clinical protocols. Enalapril was frequently discussed at Warner-Lambert, and Warner-Lambert attempted to attend and monitor public presentations on enalapril that Merck gave from time to time. Murthy 372:24-373:7; 375:19-376:20.

For example, in ***1981***, Warner Lambert:

- decided upon its capsule sizes for quinapril's clinical studies based in part on the recommended dosage forms for enalapril (Murthy 370: 1-14; DTX 17, at WL 46226);
- postponed naming its active ingredient "quinapril" — at the time it was referred to only as CI-906 — pending the disclosure of the name of Merck's MK-421 (enalapril) product (Murthy 371:16-373:24; DTX 17, at WL 46228; DTX 18, at WL 46229);
- noted that there were few unique features to distinguish the quinapril compound from enalapril in pharmacology studies (Murthy 373:8-18; DTX 18, at WL 46230); and
- monitored published studies regarding enalapril to determine assay methodology for quinapril. Murthy 370:15-371:9; DTX 17, at WL 46228.

In ***1982***, Warner-Lambert:

- forecasted that enalapril would have sales of $100 million by 1985. Murthy 374:10-14; DTX 21, at WL 46237.

In ***1984***, Warner-Lambert:

- learned that Merck's enalapril NDA would be presented at a public meeting and attended the meeting (Murthy 375:19-377:3; DTX 24, at WL 46288);

- reviewed the contents of the quinapril NDA in light of what was learned at these meetings (Murthy 375:19-377:9; DTX 24, at WL 46288); and

- was unable to persuade Tanabe, a Japanese pharmaceutical company, to license quinapril because Tanabe believed that the quinapril data was "not remarkably different than enalapril." Murthy 375:9-15; DTX 24, at WL 46287.

In ***1985***, Warner-Lambert:

- analyzed the package insert for Merck's enalapril product sold in Germany to design congestive heart failure studies for quinapril (DTX 30, at WL 21400; Murthy 380:5-20);

- designed severe hypertension clinical studies where quinapril would be compared with enalapril (DTX 30, at WL 21400); and

- concluded that more data directly comparing quinapril and enalapril were needed in hypertension clinical studies. DTX 34, at WL 46303.

Merck ultimately won the race for the second 'pril and beat Warner-Lambert by a significant margin: Merck launched Vasotec in January 1986. Murthy 381:23-382:2; DTX 117; Brenner 134:13-18. Warner-Lambert would not launch its U.S. quinapril formulation (Accupril) until 1991, five years later. Harris 124:1-3.

2. Warner-Lambert Continued to Analyze Vasotec after Vasotec's U.S. Launch in January 1986.

Warner-Lambert's interest in enalapril intensified after Merck launched Vasotec in the U.S. in January 1986; Warner-Lambert management pressured its scientists to develop a stable quinapril formulation as soon as possible. Murthy 382:17-383:8. To this end, Warner-Lambert management mobilized a Quinapril Product Development Team that included all of the named inventors of the '450 patent. Murthy 382:3-16; Harris 43:20-44:7. The team sought to develop a quinapril formulation that would be stable for a shelf-life of at least two years. Harris 43:14-25; 102:10-103:4.

Dr. Murthy and his colleagues knew that enalapril and quinapril were structurally similar (Murthy 407:4-6) and studied Vasotec closely. Throughout 1986, the Quinapril Product Development Team reviewed Merck publications on enalapril and analyzed Vasotec in their quest to produce a stable quinapril formulation. They did not compare their quinapril formulations to any other commercial product during this development. Murthy 406:6-407:7.

- **Obtaining The Vasotec Package Insert and Samples: January 1986**

On January 20, 1986, the head of the Quinapril Product Development Team at the Ann Arbor Warner-Lambert site distributed a copy of the Vasotec package insert to Dr. Murthy. DTX 117, at WL 74411; Murthy 390:4-391:3. The package

insert listed a number of Vasotec's excipients: "In addition to the active ingredient enalapril maleate, each tablet contains the following inactive ingredients: iron oxides, lactose, magnesium stearate, starch, and other ingredients." DTX 117, at WL 74412. Therefore, early in 1986, Dr. Murthy knew that Vasotec contained lactose (Murthy 391:16-22) and that Vasotec was made by mixing enalapril and various excipients together. Murthy 492:15-24.

- **Testing Hygroscopicity: March 1986**

Dr. Murthy also received samples of Vasotec obtained from a pharmacy in early 1986. Murthy 389:12-390:2. Because the absorption of moisture can destabilize tablet formulations, Dr. Murthy conducted moisture absorption (hygroscopicity) studies on the Vasotec samples. He compared Vasotec to various quinapril tablet formulations in March 1986, and subsequently tested the degree to which quinapril tablets degraded following exposure to moisture. DTX 35, at WL 49288; DTX 43; Murthy 397:20-398:25; 399:23-403:1.

- **Understanding the Role of Sodium Bicarbonate, Magnesium Carbonate, and pH: May 1986–January 1987**

By May 1986, Dr. Murthy and the other Warner-Lambert scientists knew that Vasotec contained sodium bicarbonate — an alkalizing agent that would raise pH.[2] Murthy 392:24-393:9; DTX 47. Dr. Murthy also knew that sodium

[2] Sodium bicarbonate is also an alkali metal salt and, under the Federal Circuit's claim construction in the moexipril case, an alkali metal carbonate.

bicarbonate was a stabilizer in Vasotec; he studied Vasotec and relied on what he learned about Vasotec when he tried to stabilize quinapril using alkalizing agents by adjusting various formulations to pre-selected pH levels. Murthy 419:17-420:3; DTX 47.

Dr. Murthy and others at Warner-Lambert conducted studies comparing the pH of Vasotec and quinapril tablets that were suspended in water and discovered that Vasotec had a pH of 6.5. Murthy 403:9-404:17; 422:12-424:2; DTX 47; DTX 45, at WL 111286; DTX 53, at WL 111456, 111460. Knowing (1) that unbuffered quinapril in solution had a low pH between 2 and 3 (Harris 51:17-20) and (2) that pH had a significant effect on stability (DTX 20; Murthy 414:10-21; DTX 40, at WL 36655; Murthy 415:20-416:20), Dr. Murthy hypothesized in a May 7, 1986, memo that if the pH of a quinapril tablet formulation could be raised by adding an appropriate amount of sodium bicarbonate, stability might be achieved. DTX 47; Murthy 418:17-419:15.

Dr. Murthy chose the pH of 6.5 — the pH of Vasotec — as one of two experimental pH points to stabilize quinapril formulations using sodium bicarbonate. Murthy 421:1-422:11. In other words, Dr. Murthy attempted to stabilize quinapril against cyclization by mixing quinapril with enough of the same stabilizing excipient used in Vasotec (sodium bicarbonate) to raise the pH of quinapril to that of Vasotec (6.5), noting: "[a]lso Vasotec (Merck's enalapril

maleate) tablets are formulated to have a pH of 6.5 through the inclusion of sodium bicarbonate." DTX 47.[3]

Although the Warner-Lambert scientists testified that these pH adjustment experiments with sodium bicarbonate and quinapril were ultimately unsuccessful (Harris 55:16-56:1), in fact they never abandoned the idea that pH affected quinapril's stability even after Warner-Lambert had settled on its quinapril formulation incorporating magnesium carbonate and lactose as stabilizing excipients. On January 14, 1987, five weeks before the filing of the '450 patent

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[3] That Dr. Murthy believed — even if he was not positive — that sodium bicarbonate functioned as a stabilizer in Vasotec was also clear from deposition testimony put to Dr. Murthy at trial:

> Q: "First of all, aside from talking among yourself, did you ask your patent attorney whether or not Vasotec was relevant as you have used the word?" And then there's an objection from Mr. O'Malley. And then this is the answer you gave, Doctor. "***As far as I am aware, Vasotec was used, sodium bicarbonate was used in Vasotec as a stabilizing agent.*** And when we tried it didn't work. So we didn't see this particularly as relevant." Do you see that testimony?
>
> A: Yes.
>
> Q: And that was accurate testimony when you gave it, wasn't it, Doctor?
>
> A: Well, what I'm saying is, that sodium bicarbonate may have been present in Vasotec as a stabilizing agent. It's just that I'm not sure.

Murthy 494:16-495:6 (emphasis added).

application, one of the inventors, Mr. Reisch, authored a memo discussing the necessity of additional experiments to evaluate the "pH effect" on the quinapril formulation. DTX 65, at WL 029202. Dr. Harris confirmed at trial that these investigations — undertaken by Mr. Waldman, another named inventor, in late January 1987 (PTX 209, at WL 27341-43) — were directed to determining if pH could be ruled out as a link to the stabilization of quinapril. Harris 116:2-16. Dr. Murthy admitted at trial that by late January 1987, the inventors had still not ruled out pH as the mechanism of stabilization. Murthy 436:5-8.

Dr. Harris also confirmed his prior deposition testimony that the quinapril / magnesium carbonate formulation was stable ***because*** of the pH of the composition. Harris 117:1-118:7. Even if the inventors were not absolutely certain that sodium bicarbonate stabilized Vasotec, they knew that sodium bicarbonate raised pH, and under their prevailing theory, pH was an important factor in stabilization.

- **Understanding that Enalapril Cyclizes: September 1986**

Based on their knowledge of the structural similarity between quinapril and enalapril, by the time the inventors tried to stabilize quinapril using the same ingredient they knew to stabilize Vasotec, the inventors either knew or theorized that enalapril — like quinapril — cyclized. Murthy 512:25-513:10. They certainly knew this by September of 1986. Murthy 413:2-14. In a Warner-Lambert patent

application prepared in September of 1986, teaching the stabilization of ACE inhibitors against cyclization using ascorbic acid, the same inventors told the PTO that enalapril and quinapril are both subject to cyclization. Murthy 409:19-413:7; DTX 231; DTX 377. Because Merck had launched its Vasotec product, Dr. Murthy also knew that Merck had successfully stabilized enalapril against cyclization. Murthy 448:15-17; 492:1-493:8.

- **Reviewing Merck Articles About Vasotec: September–December 1986**

Between September and December 1986, Merck scientists published Bohidar et al. and Shiromani et al. in *Drug Development & Industrial Pharmacy*. Murthy 388:22-389:11; Schwartz 263:7-15. Dr. Murthy made it his practice to review this journal as part of his work on quinapril (Murthy 385:1-21) and he read these two articles prior to the filing of the '450 patent application. Murthy 385:22-389:10; 453:1-21; 385:9-13; 457:23-458:23.

The first article, Bohidar et al., was written by three authors, two of whom Dr. Murthy knew in 1986 to have been working on enalapril at Merck. Murthy 454:22-25. This article disclosed that sodium bicarbonate can be used to prevent cyclization of a drug substance known to cyclize at low pH. DTX 259, at TP 50711; Murthy 455:1-13; 456:11-457:22. Although Bohidar et al. does not specify the drug that was being studied, Dr. Murthy admitted at trial that he knew that the unnamed drug was enalapril. Murthy 455:24-456:2. Indeed, at the time Dr.

Murthy read Bohidar et al., enalapril and quinapril were the only two drugs Dr. Murthy knew to degrade via cyclization. Murthy 453:11-12; 454:21-455:13.

The second article, Shiromani et al., also by the same two Merck authors known by Dr. Murthy, confirmed that ***enalapril*** is susceptible to cyclization. DTX 38, at WL 30576. Shiromani et al. focused on hygroscopicity studies, suggesting that moisture had an effect on enalapril stability. These studies were similar to experiments previously conducted by Dr. Murthy in March 1986 comparing the hygroscopicity of Vasotec to quinapril tablets in stability studies. Dr. Murthy considered this second Merck article important enough to bring to the attention of co-inventor Dr. Harris. DTX 38; Murthy 458:2-459:23.

These two Merck articles published in *Drug Development and Industrial Pharmacy* confirmed to Dr. Murthy what he and the other Warner-Lambert scientists already knew based on almost a year of analysis: that sodium bicarbonate was used to stabilize enalapril against cyclization in Vasotec.

- **Cumulative Knowledge Gleaned From Monitoring Merck's Product and Publications: January 1986–February 1987**

Based on their monitoring of Vasotec throughout the development of their quinapril product, by the time the inventors filed their application for the '450 patent, they were well aware that:

- Vasotec contained enalapril (Murthy 448:10-13; 491:14-492:6);

- Enalapril was an ACE inhibitor susceptible to cyclization (Murthy 448:10-13, 492:7-10);
- Vasotec was made by having its ingredients mixed together (Murthy 492:15-19);
- Vasotec included sodium bicarbonate as a stabilizer (Murthy 491:14-19);
- Vasotec contained lactose (Murthy 391:16-392:5; 506:8-13);
- Merck had solved its degradation problem because Vasotec was on the market and therefore had received FDA approval (Murthy 448:10-18; 493:5-8); and
- Merck had successfully stabilized its enalapril formulation, containing sodium bicarbonate and lactose, against cyclization before Warner-Lambert had done so with quinapril. Murthy 492:15-493:8.

3. The Development of Quinapril Culminated in the Filing of an Overreaching Patent Application That Encompassed Vasotec.

On February 24, 1987, Warner-Lambert's patent attorney, Ronald Daignault, filed the '450 patent application. DTX 1. Dr. Murthy and the other inventors personally assisted Mr. Daignault in drafting this application (Murthy 460:20-22), and provided whatever information was needed about the invention to Mr. Daignault. Murthy 460:20-22; 462:5-19; 475:18-25. Mr. Daignault relied on the inventors to provide all of the pertinent scientific information, because he had no knowledge of the invention apart from what the inventors provided. Murthy 462:16-463:1.

At the time the application was filed, Dr. Murthy had two previous patent applications under his belt. Murthy 460:20-461:5. He knew that patents were not granted automatically, but would be examined by the PTO. Murthy 461:6-13. He also knew that to obtain a patent, the invention must be new and inventive, and that no one could have made the same invention before. Murthy 461:21-25. Furthermore, he knew that if the invention was not new or inventive, the application could be rejected. Murthy 462:1-4. Most importantly, Dr. Murthy knew that he owed a duty of candor in the prosecution of his patent application (Murthy 476:15-478:9) and Mr. Daignault reminded him of the duty of inventors to disclose all relevant prior art to the PTO. Murthy 476:15-478:9.

Dr. Murthy and the other inventors reviewed drafts of the patent application. Murthy 463:1-7. In early February 1987, the inventors signed a declaration in which Dr. Murthy and each of his four co-inventors swore that:

- he believed that he was the first, ***original***, and joint ***inventor*** of the subject matter claimed and for which a patent was sought;
- he ***reviewed and understood the contents of the specification***, including the claims;
- he ***acknowledged the duty to disclose*** information material to the examination of the application; and
- he ***understood that willful false statements may jeopardize*** the validity of any patent issued from the application.

DTX 2, at 22 (emphasis added). Drs. Murthy, Harris, and Hokanson and Mr. Reisch had each signed such an oath at least twice before. Murthy 464:12-466:5; DTX 377; DTX 231; DTX 232.

The '450 patent specification that the inventors read, understood, and the subject matter of which they swore they invented, included the following original claims 1, 12, 18, and 19:

1. A pharmaceutical composition which contains:

   (a) a drug component which comprises an ***ACE inhibitor*** which is susceptible to cyclization, hydrolysis, and discoloration,

   (b) a suitable amount of a ***metal containing stabilizer*** to inhibit cyclization and discoloration, and

   (c) a suitable amount of a ***saccharide*** to inhibit hydrolysis.

12. The composition of Claim 1 wherein (a) is ***enalapril*** or a pharmaceutically acceptable acid addition salt thereof.

18. A process for stabilizing an ***ACE inhibitor*** drug against cyclization which comprises the step of contacting the drug with:

   (a) a suitable amount of an ***alkali or alkaline earth-metal salt*** and,

   (b) one or more ***saccharides***.

19. The process of Claim 18 wherein the drug is selected from the group consisting of quinapril, ***enalapril***, and indolapril, or a pharmaceutically acceptable acid addition salt thereof.

DTX 3, at WL 35941-43 (emphasis added).

Claims 18 and 19 plainly covered Vasotec, a formulation that included enalapril (an ACE inhibitor), sodium bicarbonate (a metal-containing stabilizer and alkali metal salt), and lactose (a saccharide). Vasotec was clearly implicated in claims 1 and 12 as well. The inventors knew that Merck developed the Vasotec formulation before they developed their quinapril formulation. DTX 117; Murthy 381:22-382:7; 492:15-493:8. Nevertheless, neither Dr. Murthy nor any of his co-inventors ever informed Mr. Daignault or the PTO about the existence of Vasotec, any literature about Vasotec,[4] or its pertinence to the claims recited in the application.

B. Warner-Lambert Intentionally Failed to Inform the PTO About Vasotec — Which Was "Highly Material" Prior Art — and Therefore Committed Inequitable Conduct that Renders the '450 Patent Unenforceable.

The undisputed facts require the conclusion that Warner-Lambert intended to deceive the Patent Office. When combined with the Court's previous finding that Vasotec was material to the '450 patent, that conclusion compels a finding that the '450 patent is unenforceable due to inequitable conduct.

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[4] Of the references mentioned above and discussed *infra* as being invalidating prior art, the trial testimony clearly shows that Dr. Murthy knew about Bohidar et al. and Shiromani et al., and the Vasotec package insert, but failed to disclose any of these references to his patent attorney or to the PTO. Murthy 385:22-389:10; 390:4-391:3; 453:1-21; 385:9-13; 457:23-458:23.

1. The Higher the Level of the Materiality of the Withheld Information, the Lower the Level of Intent Required.

Inequitable conduct is an issue of law based on two factual findings: (1) materiality, *i.e.*, an affirmative misrepresentation of material fact, a failure to disclose material information, or a submission of false material information; and (2) an intent to deceive. *Critikon, Inc. v. Becton Dickinson Vascular Access, Inc.*, 120 F.3d 1253, 1256 (Fed. Cir. 1997). While materiality and intent must be established by clear and convincing evidence (*id.*), if the withheld information is highly material, less evidence of intent is necessary to support a finding of inequitable conduct. *Elk Corp. of Dallas v. GAF Bldg. Materials Corp.*, 168 F.3d 28, 32 (Fed. Cir. 1999). "The more material the omission or the misrepresentation, the lower the level of intent required to establish inequitable conduct, and vice versa." *Critikon*, 120 F.3d at 1256.

2. As This Court Has Already Found, Vasotec Was Highly Material Prior Art.

This Court has already held that Vasotec was "highly material," to the application for the '450 patent, *i.e.*, there was a substantial likelihood that a reasonable examiner would have considered it important in deciding whether to allow the application to issue as a patent. S.J. Op., at 38, 49. To the extent that the Court reconsiders that finding — and Warner-Lambert has provided absolutely no reason to do so — the essentially undisputed evidence that Vasotec fell within the

scope of the claimed invention ***confirms*** that the withheld information was highly material.[5] Nevertheless, whether such information would, in fact, invalidate the claims of the patent at issue is irrelevant to the materiality determination:

> Information concealed from the PTO may be material even though it would not invalidate the patent. *See Gardco Mfg., Inc. v. Herst Lighting Co.*, 820 F.2d 1209, 1213 (Fed. Cir. 1987) ("The simple fact is that a patent may be valid and yet be rendered unenforceable for misuse or inequitable conduct."). ... [T]he test for materiality is whether a reasonable examiner would have considered the information important, not whether the information would conclusively decide the issue of patentability. *See A.B. Dick Co. v. Burroughs Corp.*, 798 F.2d 1392, 1397 (Fed. Cir. 1986) ("The test for materiality is *not* whether there is anticipation or obviousness but, rather, what a 'reasonable examiner would consider . . . important in deciding whether to allow the application to issue as a patent.") (emphasis and alteration in original).

Li Second Family, 231 F.3d at 1380-81.

3. The Inventors of the '450 Patent Intentionally Withheld Vasotec From the PTO.

As the Federal Circuit has explained:

> No single factor or combination of factors can be said always to require an inference of intent to mislead; yet a patentee facing a high level of materiality and clear proof that it knew or should have known of that materiality, can expect to find it difficult to establish 'subjective good faith' sufficient to prevent the drawing of an inference of intent to mislead. ***A mere denial of intent to mislead (which would defeat every effort to establish inequitable conduct) will not suffice in such circumstances.***

[5] Indeed, the Federal Circuit's construction of term "carbonate" to include sodium bicarbonate in the moexipril case only enhances the materiality of Vasotec.

Critikon, 120 F.3d at 1257 (emphasis added). The Federal Circuit has also clearly stated that "'smoking gun' evidence is not required in order to establish an intent to deceive. Rather, this element of inequitable conduct, must generally be inferred from the facts and circumstances surrounding the applicant's overall conduct." *Paragon Podiatry Lab. v. KLM Lab.*, 984 F.2d 1182, 1189-90 (Fed. Cir. 1993) (citations omitted). This is so because "[d]irect evidence of intent or proof of deliberate scheming is rarely available in instances of inequitable conduct." *Critikon*, 120 F.3d at 1256. Accordingly, intent to deceive need not be, and usually is not, proven by direct evidence. *Semiconductor Energy Lab. v. Samsung Elecs.*, 204 F.3d 1368, 1374-75 (Fed. Cir. 2000).

The evidence in this case as elicited at trial clearly and convincingly exceeds the threshold level of intent required to establish inequitable conduct, particularly in the face of the high materiality of the information the inventors concealed from the PTO.

a. The Inventors of the '450 Patent Knew that the '450 Patent Application Read on Vasotec and that Vasotec Was Material

There is no question that the '450 patent application reads on an ACE inhibitor formulation made with enalapril and stabilized by mixing these ingredients with sodium bicarbonate and lactose. The inventors knew this and therefore knew of Vasotec's materiality to their application.

- **With respect to "ACE inhibitor"**

The Warner-Lambert inventors certainly knew their application encompassed enalapril and that enalapril was an ACE inhibitor. Indeed, this was the inventors' third patent application reciting enalapril (Murthy 460:23-461:9) and the third time at the inventors had signed an oath that their invention included enalapril.[6] Murthy 464:12-466:5. The patent, as Dr. Murthy acknowledged, plainly covered enalapril as well as quinapril formulations. Murthy 479:23-480:3. Enalapril is ***explicitly*** recited in original claims 12 and 19 and identified as "particularly valuable" in the '450 patent specification. DTX 3, at WL 35933; Murthy 482:13-25. Dr. Murthy admitted that enalapril fell within the scope of at least claims 1, 12, 18 and 19 as filed. Murthy 484:20-488:12; DTX 3. Furthermore, he carefully "read, reviewed and understood" the specification and the claims before the application was filed (Murthy 464:1-11; 480:6-11), and therefore must have been aware at the time of filing that the claims embraced enalapril. Dr. Murthy also knew at the time of filing that the Vasotec formulation included enalapril. Murthy 492:1-6.

- **With respect to "saccharide"**

Dr. Murthy knew that lactose was a saccharide at the time the application was filed. Murthy 488:21-23. Furthermore, he carefully "read, reviewed and

[6] Specifically, inventors Murthy, Reisch, Hokanson and Harris.

understood" the specification and the claims before the application was filed (Murthy 464:1-11; 480:6-11), and therefore must have known at the time of filing that the claims embraced lactose. Dr. Murthy also knew at the time of filing that the Vasotec formulation included lactose. Murthy 391:16-392:5; 506:8-13.

- **With respect to an "alkali metal salt"**

Dr. Murthy was well aware in 1986 that sodium bicarbonate was an alkali metal salt. He admitted at trial that even a person with only basic knowledge of chemistry would have known that sodium bicarbonate fell within the "alkali metal salt" limitation of claims 18 and 19, as filed. Murthy 363:22-364:4; 490:11-15. Furthermore, he carefully "read, reviewed and understood" the specification and the claims before the application was filed (Murthy 464:1-11; 480:6-11), and therefore must have been aware that the claims embraced alkali metal salts. Dr. Murthy also knew Vasotec included sodium bicarbonate, an alkali metal salt, and that sodium bicarbonate was the stabilizer in Vasotec.[7] DTX 47; Murthy 494:16-495:6.

The inventors also knew that enalapril was an ACE inhibitor susceptible to cyclization (Murthy 448:10-13, 492:7-10), that Vasotec was made by having its

[7] Furthermore, the inventors had no basis to determine that magnesium carbonate could stabilize enalapril. Murthy 490:25-491:25. The only alkali metal salt they knew could do so was sodium bicarbonate; therefore they must have intended that their patent application cover sodium bicarbonate. Murthy 495:13-496:2.

ingredients mixed together (Murthy 492:15-19), and that Vasotec was stable. Murthy 448:15-18; 493:5-8. Accordingly, the inventors knew that the Vasotec formulation met every limitation of claims 18 and 19 as filed. There is clear proof that the inventors should have known — and did know — that Vasotec was material to the prosecution of their patent application. *Critikon,* 120 F.3d at 1257.[8]

In light of Dr. Murthy's admitted knowledge of prosecution procedure, his knowledge of Vasotec, and his close review and understanding of the claims of the '450 patent as filed, it is impossible to conclude that Dr. Murthy did not act with an intent to deceive.

A person knowing what Dr. Murthy knew could only fail to disclose Vasotec as material if he sought to prevent the PTO from considering it.

b. The Inventors of the '450 Patent Deliberately Chose to Hide the Existence of Vasotec From Their Patent Attorney and the PTO.

In addition to the strong inference of intent based upon the inventors' knowledge of the facts that made Vasotec material to their claims, there is ***direct*** evidence supporting a finding that the decision to suppress Vasotec was made

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[8] Indeed, at trial, Dr. Murthy refused to answer a simple question as to whether he knew of any drug or publication that was closer to claims 18 and 19 than Vasotec. Murthy 505:16-508:25. This evasion spoke volumes; it is clear that the answer is "no." The inventors knew that Vasotec was the best prior art reference, and if they concealed it, the PTO would be unable to locate it and the inventors would get their patent.

consciously and deliberately.

At his deposition, Dr. Murthy clearly testified that around the time of filing, the named inventors of the '450 patent discussed the relevance of Vasotec to their patent application. They decided not to inform their patent attorney about Vasotec (Murthy 499:2-18), a decision that virtually ensured that the PTO would remain unaware of Vasotec's existence.

However, at trial, Dr. Murthy tried to back-pedal. First, he stated that the discussion among the inventors was not "formal" and that their interest in Vasotec had waned:

> Q: And there came a time, right, when you and your other inventors discussed among yourselves what to disclose to the patent attorney; right?
>
> A: Okay. Not in any formal meetings, we developed a rough draft and it was defined and —
>
> Q: Well, you had a discussion — whether the meeting was formal or not, you had a discussion with your other inventors about what to disclose with the patent attorney; isn't that right?
>
> A: I cannot recall if a formal meeting or — it may have been talked about.
>
> Q: Okay. And as part of these discussions, you hadn't forgotten about Merck's Vasotec product at the time you filed this patent application, had you?
>
> A: Well, the thing is, Merck's Vasotec was of great interest to us in the beginning of our program, but when — once we tried the sodium bicarbonate experiment, and it did not — and we were not successful, our interests waned considerably about Vasotec.

Murthy 497:6-498:1.

Then, Dr. Murthy stated that his specific recollection at his deposition that the inventors discussed whether to disclose Vasotec to their attorney was an error, and denied that such a discussion had ever occurred:

> A: [I]t's true that I — I did testify to this effect, but after reflecting on it, it just — I was mixed up with the dates at the time. It was true, we did discuss about this, but that was the beginning of the program and not at the time of the filing.
>
> Q: Well, the question was ***whether you discussed whether to disclose Vasotec to the patent attorney who was preparing your application.*** Right, Doctor?
>
> A: Well, we — as I said, at the time of filing the patent, Vasotec was not as important as it was in the beginning of the program. In fact, it just fell off the radar screen.
>
> Q: But it's clear, Doctor, when we just read these questions, the discussions that you were referring to in your testimony were discussions that took place at or about the time the patent application was filed, isn't that right?
>
> A: Discussions regarding what?
>
> Q: Whether to disclose Vasotec to the patent attorney, and if you look at page 119, you said in answer to the question: When did these discussions take place? "ANSWER: I cannot recall a specific date, but around the time of filing."
>
> A: Yes.
>
> Q: Wasn't that referring to the filing of the patent application?
>
> A: Okay. As I said, I was mistaken as far as my — the events that surrounded, at the time of the filing of the patent. I ***cannot now recall*** having any discussions about Vasotec, or any of the products at the

time of the filing. The discussions took place much earlier, at the beginning of the program.

Q: Well, your deposition, Doctor, if you look at the first page. This deposition was taken in November of 2000; right?

A: Yes.

Q: And you're giving testimony today in May, 2004; right?

A: No. [*sic*]

Q: If you look on the first page it says November 17, 2000.

A: Yes.

Q: And wouldn't you agree with me, Doctor, that your recollection was probably better in 2000 then it is today as to what transpired at that time?

A: No, I did not — see, I began to think about this whole program at the time that I gave the deposition. I ***must have gotten mixed up*** about the — when some of these discussions took place.

Q: And you want to change now the testimony you gave at your deposition?

A: Well, I'm trying to correct the wrong, keep it straight. The discussions about Vasotec and Enalapril and sodium bicarbonate, they took place at the beginning of our efforts to stabilize, somewhere in the main — well, whenever we — whenever we started the stabilization project. What I'm saying is after the sodium — sodium bicarbonate experiments failed and it didn't help us, ***we practically lost interest*** in using Enalapril or Vasotec as any kind of guidance for our efforts.

Murthy 500:19-503:5 (emphasis added).

Serious questions of credibility are raised when a lead witness attempts on the stand to recant deposition testimony on the central issue of the trial. Neither Dr. Murthy nor Warner-Lambert's counsel ever corrected Dr. Murthy's deposition testimony in the four years between the deposition and the trial. In the intervening years, summary judgment motions — containing the same deposition testimony at issue — had been filed and adjudicated.[9] Teva relied heavily on Dr. Murthy's deposition testimony, and Warner-Lambert never advised Teva or the Court of Dr. Murthy's shift in recollection "after reflecting on it," at all. Murthy 500:19-21. Such "[s]elf-serving, revisionist testimony" cannot be used to justify a failure to disclose prior art. *Frazier v. Roessel Cine Photo Tech.*, 2003 US Dist. LEXIS 19607, at *92 (C.D. Cal. Apr. 9, 2003); *see also Molins*, 48 F.3d at 1182 ("Those who are not 'up front' with the PTO run the risk that, years later, a fact-finder might conclude that they intended to deceive").

Deposition testimony that is closer in time and less tainted by evasion and non-responsiveness is more credible than litigation-inspired trial testimony. But whether the Court chooses to believe Dr. Murthy's recanted deposition testimony

[9] Indeed, the Court must have relied on Dr. Murthy's deposition testimony for the following finding: "The Warner-Lambert scientists discussed the applicability of Vasotec to the '450 patent application which they were about to file. They decided not to mention Vasotec to their patent counsel." S.J. Op., at p. 50. Nevertheless, Warner-Lambert failed to address the purported error in testimony until the trial.

— the rarely available direct evidence of intent — or his trial testimony, it is undisputed that Dr. Murthy did not disclose Vasotec to his patent attorney and that Dr. Murthy had knowledge of facts plainly establishing the materiality of Vasotec at the time of his dealings with that attorney.

The '450 inventors were well aware of Vasotec at the time of filing. Vasotec did not "just f[a]ll off the radar screen" (Murthy 501:5), and the inventors manifestly had not "practically lost interest in using Enalapril or Vasotec as any kind of guidance." Murthy 503:1-5. Dr. Murthy's persistent interest in Merck's product is evidenced by the fact that he considered Merck's Shiromani et al. article important enough to bring to co-inventor Dr. Harris' attention, even though this article was not published until the end of 1986. DTX 38; Murthy 458:2-459:23; Schwartz 263:7-15.

Furthermore, it is not credible that the self-avowed "first and original inventors" of a stabilized enalapril formulation could have lost "interest in using Enalapril ... as any kind of guidance" by the time they made the claim to have invented such a formulation. Murthy 503:1-5. Nor could they have failed to consider Vasotec material prior art when their study of Vasotec was the ***only*** basis on which they could have concluded that sodium bicarbonate stabilized enalapril, as they claimed in the patent. Murthy 448:19-449:2. The inventors had no means of even acquiring enalapril isolated from the other ingredients in Vasotec. Murthy

514:13-16. They had no means of quantifying enalapril degradation products, lacking the necessary assay procedures that were proprietary to Merck. Murthy 402:16-403:1; 490:22-24. Indeed, Dr. Murthy admitted that the inventors did not run any experiments that could form the basis of their patent application to the extent it pertained to enalapril. Murthy 480:16-20; 490:17-21. Therefore, whatever the inventors knew of enalapril came from Vasotec and Merck publications and not from any inventive activity on their part. Their failure to disclose Vasotec to the examiner was a conscious act of suppression, not a lapse of memory.

"It is axiomatic that 'close cases should be resolved by disclosure, not unilaterally by applicant.'" *GFI, Inc. v. Franklin Corp.*, 265 F.3d 1268, 1274 (Fed. Cir. 2001) (citation omitted). In this case, the question was not even close. Even if it had been, there was a patent attorney available to the inventors to whom they could have directed any questions. Murthy 503:23-504:5. The Federal Circuit has stated that:

> [O]ne ***should not be able to cultivate ignorance, or disregard numerous warnings that material information or prior art may exist, merely to avoid actual knowledge of that information or prior art. Where one does, deceptive intent may be inferred.*** Once an attorney, or an applicant, has notice that information exists that appears material and questionable, that person cannot ignore that notice in an effort to avoid his or her duty to disclose.

Brasseler, U.S.A. v. Stryker Sales Corp., 267 F.3d 1370, 1383 (Fed. Cir. 2001) (citations omitted).

Thus, the Court may properly infer the requisite intent to mislead upon a showing that an applicant has cultivated his or her own ignorance in the face of potentially material information. *Id.* at 1383; *FMC Corp. v. Hennessy Indus.*, 836 F.2d 521, 526 n. 6 (Fed. Cir. 1987).

At a minimum, upon reviewing the claims of the '450 patent clearly embracing Vasotec, the inventors should have asked their patent attorney whether to disclose Vasotec. At some point, they collectively chose not to do so. Murthy 504:13-22. This failure even to ask constitutes cultivation of ignorance, and is evidence, in and of itself, of deceptive intent. *Brasseler,* 267 F.3d at 1385.

4. Warner-Lambert Offers No Plausible Justification For the Conduct of the Inventors of the '450 Patent.

Where withheld information is material and the patentee knew or should have known of that materiality, the patentee can expect to have great difficulty in establishing subjective good faith sufficient to overcome an inference of intent to mislead. *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 326 F.3d 1226, 1239 (Fed. Cir. 2003). Here, Warner-Lambert has offered no credible evidence of good faith to counter the strong evidence of an intent to deceive the PTO. In fact, the justifications offered by Warner-Lambert are no excuses at all.

a. "Sodium Bicarbonate Fell Off the Table" is No Excuse.

To justify his nondisclosure of Vasotec to the PTO, Dr. Murthy testified at trial that at some point in the development of quinapril in 1986, "sodium bicarbonate fell off the table." Murthy 441:2-24. This testimony is simply not accurate. The '450 patent inventors had an ongoing interest in a "pH effect" because there was a desire to raise the pH of quinapril in the same manner that sodium bicarbonate raised the pH of Vasotec. DTX 65, at WL 029202; DTX 20; Murthy 414:10-21; DTX 40, at WL 36655; Murthy 415:20-416:20; DTX 47; DTX 53, at WL 111540. The evidence demonstrates that this interest in sodium bicarbonate continued up to the time the '450 patent application was filed.

First, even after Warner-Lambert undertook its allegedly unsuccessful pH adjustment experiments with sodium bicarbonate, Imperial Chemical Industries ("ICI") — a company with which Warner-Lambert had been collaborating to develop a stable quinapril formulation — suggested to Warner-Lambert that magnesium carbonate — ***and sodium bicarbonate*** — had a "considerable stabilizing effect" on quinapril in humid conditions. DTX 58, at WL 36692. ICI came to this conclusion after engaging in excipient compatibility studies, which was the conventional approach to identifying appropriate stabilizers, in contrast to Warner-Lambert's pH adjustment approach. ICI's report must have been persuasive to the Warner-Lambert scientists (DTX 57, at WL 036699); Warner-

Lambert took the magnesium carbonate suggestion, which ultimately resulted in their stable commercial formulation.

Second, in response to a request from his supervisor, Dr. Braun, to identify alternatives to magnesium carbonate to stabilize quinapril formulations, Dr. Murthy identified sodium bicarbonate as one such alternative in a memo dated December 19, 1986. DTX 287, at WL 37605. In contrast with several other excipients identified in that memorandum, Dr. Murthy did not tell Dr. Braun that sodium bicarbonate failed to stabilize quinapril, confirming that Dr. Murthy had not ruled it out as a stabilizer. Murthy 445:7-20.

Third, the inventors continued their Vasotec- and sodium bicarbonate-inspired pH testing of quinapril through the beginning of 1987, just weeks before the filing of the '450 patent application. On January 14, 1987, Mr. Reisch authored a memo discussing the necessity of additional experiments to evaluate the "pH effect" on the quinapril formulation. DTX 65, at WL 029202. These tests were undertaken by Mr. Waldman in late January 1987. PTX 209, at WL 27341-43.

Fourth, Merck's use of sodium bicarbonate as a stabilizer for enalapril — which the inventors expressly claimed in their application — had certainly been successful at the time the '450 patent was filed. DTX 117; DTX 47. The inventors knew that enalapril cyclized and believed that sodium bicarbonate inhibited its

cyclization. Murthy 448:3-13; 455:1-13; 456:11-457:22; 494:16-495:6; DTX 47; DTX 259, at TP 50711.

Accordingly, when the inventors filed their patent application, sodium bicarbonate was very much "on the table."

b. "In [Dr. Murthy's] View Bohidar Was Not Prior Art" is No Excuse.

Counsel for Warner-Lambert suggested at trial that Dr. Murthy's failure to disclose Bohidar et al. and Shiromani et al. to the PTO was a nullity because these references were not "prior art," relative to the time when Dr. Murthy thought the inventors had solved the problem of quinapril stability. Murthy 535:15-21. That is no excuse for the failure to disclose Vasotec itself.

As an initial matter, it was not for the inventor to make the legal determination of whether the requirements for establishing a conception date in advance of patent filing had been met. "As a general matter, upon filing of an application, the application date becomes the applicant's presumed invention date." *Frazier,* 2003 US Dist. LEXIS 19607, at *94. Thus, Bohidar et al. should have been disclosed.

Regardless, Dr. Murthy knew that Merck had developed a stable enalapril formulation — discussed in Bohidar et al. — ***prior*** to publication of Bohidar et al. and Shiromani et al. because he knew that Merck launched Vasotec in January 1986. The Vasotec launch, and information learned subsequently, put Dr. Murthy

(and the other inventors) on notice that the invention had been " 'known or used by others' prior to [their] application date, *i.e.*, [their] presumptive date of invention." *Id.* at *94.

As will be demonstrated *infra* in Teva's invalidity arguments, the prior invention of Vasotec, a stable enalapril formulation referred to in Bohidar et al. and Shiromani et al., ***was***, in fact, prior art to the '450 patent application. For the inventors to have overcome a rejection in the patent office, it would have been necessary to "independently establish a date of invention in the United States prior to the date that [Vasotec and the Vasotec process were] first known or used by others." *Id.* at *94. By failing to disclose Vasotec, the inventors successfully avoided having to make this showing. *Id.* The successful avoidance also "applie[d] under 35 U.S.C. § 102(g)(2),[10] which provides for a rejection where another has made the invention in the United States before the applicant." *Id.* The inventors therefore suppressed material information.

c. "Patent Attorneys By Nature Try and Claim the World" is No Excuse.

Counsel for Warner-Lambert suggested at trial that no inequitable conduct occurred because "patent attorneys by nature try to claim the world." Murthy 540:14-17. That is no excuse. The fact that it was the lawyer who drafted the

claims encompassing Vasotec does not absolve the inventor whose duty it was to disclose information relevant to claims that were read and understood in several iterations. Furthermore, as to patent counsel's hypothesized tendency to "claim the world" — it is unclear how Dr. Murthy would have been able to make such a sweeping generalization — even if Dr. Murthy had a basis for reaching such a conclusion, it does not absolve Dr. Murthy or his employer, Warner-Lambert, of their disclosure obligations. *FMC Corp. v. Manitowoc Co.*, 835 F.2d 1411, 1415 n.8 (Fed. Cir. 1987) ("[T]he knowledge and actions of applicant's attorney are chargeable to applicant.").

If anything, Dr. Murthy's claimed awareness of patent lawyers' tendency to "try and claim the world" should have made him more vigilant against a known inclination to misrepresent the scope of the claimed invention. Dr. Murthy — unlike Mr. Daignault — knew that the claims were drafted broadly enough to encompass a product developed by Merck before he and his colleagues had succeeded in developing a stable quinapril formulation. Having claimed that he had invented Merck's process for stabilizing an enalapril formulation, it was incumbent on Dr. Murthy to disclose that prior art formulation in connection with the prosecution of that claim.

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[10] As will be discussed, *infra,* this statute provides that a patent cannot be granted on an invention that was previously made in this country by another inventor who had not abandoned, suppressed or concealed it.

Accordingly, Warner-Lambert cannot establish " 'subjective good faith' sufficient to prevent the drawing of an inference of intent to mislead. A mere denial of intent to mislead (which would defeat every effort to establish inequitable conduct) will not suffice in such circumstances." *Critikon*, 120 F.3d at 1257.

5. Dr. Murthy's Evasiveness Confirms The Inventors' Intent To Deceive.

Particularly when the central issue of a case rests on a question of intent, the purpose of a trial is to allow the Court to assess the credibility of *viva voce* witnesses. *See e.g. GFI, Inc. v. Franklin Corp.*, 88 F. Supp. 2d 619, 626 (N.D. Miss. 2000) ("In short, in light of all the circumstances and surrounding facts including the demeanor and credibility of the witnesses that testified during this trial, the court, in balancing the evidence, finds that the Plaintiff engaged in inequitable conduct..."); *see also Key Pharms. v. Hercon Labs. Corp.*, 161 F.3d 709, 719 (Fed. Cir. 1998) (finding no clear error in an inequitable conduct analysis because "the finding on intent in particular depended heavily on the presentation of evidence and witness testimony at trial. The trial court was able to hear these matters first hand and assess witness credibility"). Rather than being candid, direct, and plainspoken, Dr. Murthy was evasive and deliberately non-responsive on questions concerning Vasotec and its non-disclosure to the PTO.

For example, when asked about his understanding that his patent application included enalapril, Dr. Murthy was evasive:

Q: You testified yesterday that before you signed your declaration, you had read and understood the specification and the claims in the patent. Do you recall that testimony?

A: Yes.

Q: Okay. So did you understand at that time, Doctor, that your patent was directed not only to formulations contained in Quinapril, but also formulations containing Enalapril?

A: ***Our focus — our focus was on Quinapril, and I have to read this closely to see, but Enalapril was included. We worked on Quinapril. We did not work on Enalapril. We didn't run any experiments that forms the basis. I just have to look at it closely now. I have to read it closely. Can you show me where it says — discussing —***

Q: I will, Doctor. You read it closely at the time you signed your application, right, Doctor?

A: Yes.

Murthy 480:6-25 (emphasis added); *see also* Murthy 486:18-488:1. Dr. Murthy never stated that he was ***not*** aware that his patent application included enalapril, nor could he, having testified that he read the application closely at the time. Murthy 480:23-25.

Having testified earlier in the day that he knew Drs. Shiromani and Bavitz were working on Merck's enalapril (Murthy 386:24-387:7), Dr. Murthy was evasive when asked the same question in the context of his knowledge of sodium bicarbonate's function in Vasotec:

Q: And you knew that the authors of this article were writing — or working on Merck's Enalapril product; right?

A: It's — it's a reasonable guess, but they he did not say that in the article.

Q: I'm sorry — the question, Doctor, you knew that Dr. Bavitz and Shiromani — Shiromani, were working on Merck's Enalapril product; correct? I think you testified to that — to that earlier today.

A: Yes.

Murthy 455:14-23.

Dr. Murthy easily answered questions of basic chemistry about alkali and alkaline earth metals until the subject turned to sodium bicarbonate. For example:

Q: And now magnesium salt is a salt of a group 2 metal; is that right?

A: Yes.

Q: It is therefore an alkaline earth metal salt; right?

A: Yes.

Q: And magnesium carbonate is an example of such a salt; correct?

A: Yes.

Q: Now, a potassium salt is a salt of a group 1 metal; correct?

A: Yes.

Q: And it is therefore an alkali metal salt; correct?

A: Yes.

Q: And potassium phosphate is an example of such a salt; right?

A: Yes.

Q: A sodium salt is a salt of a group 1 metal; right?

A: Yes.

Q: And it is therefore an alkali metal salt; right?

A: Yes. Yes.

Q: And sodium bicarbonate, sodium bicarbonate is an alkali metal salt; right?

A: ***Are you — in what context are you asking?***

Q: The question is, is sodium bicarbonate an alkali metal salt? Is that a correct statement, Doctor?

A: Yes.

Murthy 363:1-364:2. The same thing happened the following day. Dr. Murthy was asked:

Q: And then as you testified yesterday, magnesium carbonate is an example of an alkaline earth metal salt; right?

A: Yes.

Q: Okay. And as you testified yesterday, sodium bicarbonate is an example of an alkali metal salt; right?

A: Well, okay. We do not — we did not have in mind sodium bicarbonate, otherwise we would have been very specific about it. Because our experiments with sodium bicarbonate did not help us in the stabilizing of Quinapril. ***So we didn't — at least I did not have in mind sodium bicarbonate and to prevent cyclization of Quinapril.***

***

Q: Anyone with a basic knowledge of chemistry understands that sodium bicarbonate is an alkali metal salt; correct?

A: I mean, I have difficulty in this context to accept that, because were we — our experiments with sodium bicarbonate were unsuccessful —

THE COURT: And, Doctor Murthy, he's directing you to answer not specifically to this claim, but just to the general chemical proposition.

A: Okay. Then I accept it.

Murthy 488:25-489:15; 489:25-490:9 (emphasis added).

Dr. Murthy was equally evasive when asked whether he knew of any information more material to his patent claims than Vasotec, resorting to non-responsive answers:

Q: And was there any information more material, as far as you knew, in the entire world to this — to these claims that Merck's Vasotec product —

A: You're saying other than Quinapril?

Q: Yes.

A: ***I mean — I can only say this. That we — we were focusing on Quinapril and stabilization of Quinapril, and this patent was written up with that in mind, and whatever — whatever, to Enalapril, I mean — to me they were not central to this patent.***

Q: Just a slightly different question, Doctor. You knew you had a duty to disclose material information pertinent to the patent application; right?

A: Yes.

Q: And isn't it true, Doctor, that there was nothing that you knew about anywhere that was more material to this patent application then Merck's Vasotec product; isn't that true?

A: When you say material, what do you have in mind.

Q: Well, Doctor, I'm asking you what you thought. You testified earlier that the attorney explained to you what that duty to disclose material information encompassed; isn't that right? You understood that duty, isn't that right, Doctor?

A: No. You are talking about events that took place almost 18, 19 years ago, and I don't know what they discussed. ***I mean, all I can state is this whole patent case, written with the Quinapril in mind, and that's the way I understood it.***

Q: I understand that's your testimony, Doctor. It's just a little bit different questioning. I understand what you thought about the patent, but you also understood that you had a duty to disclose material information to enable the patent examiner to determine whether these claims were sufficiently inventive to be entitled to patent protection. Didn't you testify to that yesterday? You understood that; right?

A: Yes.

Q: And so you knew you had to gather together whatever information you had to allow the patent examiner to reach a conclusion as to whether you were entitled to a patent; right?

A: Yes.

Q: So simple question, was there anything that you can think about that you thought about at the time that was any more material than Merck's Vasotec product?

MR. O'MALLEY: Your Honor, I'll object —

THE COURT: I'm going to stop this line of questioning.

Murthy 507:2-508:25 (emphasis added).

Dr. Murthy's "evasive testimony," and the fact that he "tiptoe[d] around the truth," regarding his knowledge of Vasotec and the scope of his patent application support the conclusion that his answers lack candor. *Brasseler,* 267 F.3d at 1384-

85. Related testimony supporting the absence of any intent to deceive therefore should also be viewed with "great skepticism." *Id.* at 1384; *Semiconductor Energy Lab. v. Samsung Elecs.*, 4 F. Supp. 2d 477, 488-89 (E.D. Va. 1998) (holding that a witness changing deposition testimony at trial was not credible).

Further damaging to Dr. Murthy's credibility was his belated attempt, discussed above, to repudiate his deposition testimony. On the stand, Dr. Murthy claimed that his specific recollection, under oath, four years earlier, must have been mistaken. His attempt to revise history by recanting deposition testimony taken four years closer to the date of the meeting than his trial testimony was litigation-inspired, and not credible. Warner-Lambert would have the Court believe that Dr. Murthy, (a) a Ph.D.; (b) whose post-secondary education was all in the United States; (c) who writes impeccable English in his documents; and (d) spoke English fluently in response to questions by Warner-Lambert's counsel, was "mixed up" (Murthy 500:20; 502:17; 544:8-11; 544:21-545:9) when he clearly testified that he had a discussion with his co-inventors about whether to disclose Vasotec to their patent attorney, "around the time of filing."

Dr. Murthy's change of heart casts doubt on the remainder of his testimony and his propensity for veracity at the critical time. *See Kearns v. Ford Motor Co.*, 114 F.R.D. 57, 62-63 (E.D. Mich. 1987) (holding that a witness who played semantic games, tried to avoid answering many questions, with failed recollection

and whose answers at trial differed from his answers at deposition lacked candor and credibility, "suggest[ing] to the court that much of his testimony cannot be believed.").

Dr. Murthy's demeanor at trial underscores the intent to deceive the PTO in the prosecution of the '450 patent. If Dr. Murthy had nothing to hide today, he would have provided honest and forthright answers, with good faith explanations for his failure to disclose despite his duty of candor and his knowledge that Vasotec was material to his application.

6. A Finding of Unenforceability is Appropriate.

The inventors knew and understood their duty of disclosure. They declared under oath — a statutory mandate under 35 U.S.C. § 115 — that they had reviewed and understood the specification and the claims in their original application. DTX 2, at 22-24. They were aware of material information — indeed information they referred to throughout their development efforts — which they failed to disclose. The inventors withheld Vasotec with the intent to deceive the PTO, and therefore committed inequitable conduct. They are accountable to the public for their critical omission.

To add insult to injury, Dr. Murthy and the other inventors signed a false oath stating that they were the original and first inventors of a stabilized enalapril formulation when they knew that was not the case. The inventors had not

conducted a single experiment attempting to stabilize enalapril or that could have formed the basis of their patent application to the extent it pertained to enalapril. Indeed, they had no means of doing so. Murthy 480:16-20; 490:17-21; 514:13-16; 402:16-403:1; 490:22-24.

Whatever the inventors knew about enalapril came from Vasotec and information that Merck had published. Yet, they claimed to be the first and original inventors of a stabilization methodology used to make Vasotec, the existence of which they concededly knew but failed to disclose to the examiner. On this basis alone, a finding of unenforceability is appropriate. "Defendants executed a false oath and filed the same with their application in the Patent Office, claiming themselves to be the inventors of concepts conceived and developed by [others], and having been on sale more than a year prior to the application filing date. Any patent issuing from such an application, based on a false oath, is invalid too." *Sadler-Cisar, Inc. v. Commercial Sales Network, Inc.*, 786 F. Supp. 1287, 1296 (N.D. Ohio 1991) (citations omitted); *Liquid Carbonic Corp. v. Goodyear Tire & Rubber Co.*, 38 F. Supp. 520, 526 (N.D. Ohio 1941) ("The word 'patent' generally covers two concepts: invention and the certificate of ownership of the franchise granted by law to the inventor. Such certificates or letters patent are, of course, invalid if obtained on false oath by one not the inventor...").

At bottom, despite the inventors' clear knowledge that the patent claims encompass Vasotec — and that Vasotec played a prominent role in the development of quinapril — the inventors withheld the existence of Vasotec from the PTO. A finding of unenforceability is the proper remedy:

> Notwithstanding the inherent competitive pressures of the business world and the natural desire to vanquish one's competitors, patent applicants are under a duty of candor to disclose all material references to the PTO, even when embroiled in a race to be the first to secure a patent on an item. Attempting to gain an advantage over one's business adversaries by unilaterally deciding that known material references do not have to be disclosed to the PTO during the pendency of a patent application is improper.

GFI, Inc., 88 F. Supp. 2d at 626; *see ISCO Int'l, Inc. v. Conductus, Inc.*, 279 F. Supp. 2d 489, 503 (D. Del. 2003) (inferring intent based on the inventor's particular awareness of a material reference "because of its significance to his industry and his company's principal projects" and his conscious decision to withhold it from the PTO). Warner-Lambert's deliberate choice to suppress highly material prior art renders the '450 patent unenforceable.

II. Claims 16 and 17 of the '450 Patent Are Invalid.

The patent statute recognizes that patent protection is not warranted for inventions that are not novel. 35 U.S.C. §§ 102, 103. Not only does the withholding of Vasotec compel a finding of inequitable conduct, Vasotec itself —

taken alone and in combination with other Merck-related prior art — renders claims 16 and 17 of the '450 patent invalid.

A. Claims 16 and 17 are Anticipated by Merck's Prior Practice of the Vasotec Process.

1. Patents That Claim Inventions in the Prior Art are Invalid.

A patent is invalid if it teaches nothing more than what has already been disclosed by the prior art. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 781 (Fed. Cir. 1985). Anticipation under 35 U.S.C. § 102 requires that a single prior art reference disclose, either expressly or inherently, each element of the claimed invention. *See In re Cruciferous Sprout Litigation,* 301 F.3d 1343, 1349 (Fed. Cir. 2002); *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1346 (Fed. Cir. 1999). A claim is therefore invalid when a prior art reference discloses each and every claim limitation. *Atlas Powder*, 190 F.3d at 1346.

Section 102 of the patent statute defines several distinct classes of prior art, each with its own requirements. Under the class of prior art at issue in this case, 35 U.S.C. § 102(g)(2), a patent claim is invalid if the claimed invention was first made by another inventor in the United States who had not abandoned, suppressed or concealed it. Because the claims at issue are process claims, the anticipatory prior art under § 102(g)(2) is the Vasotec Process — Merck's actual manufacture

of Vasotec for commercial sale using at least the starting ingredients of enalapril maleate, sodium bicarbonate and lactose.

Unlike other classes of prior art — where public disclosure is a prerequisite — the use of a prior invention by an earlier user under § 102(g)(2) need not be publicly available at the time of that use. The non-public use of the prior invention retains its status as invalidating prior art so long as the prior user did not thereafter abandon, suppress, or conceal the invention. *Dow Chem. v. Astro-Valcour, Inc.*, 267 F.3d 1334, 1339 (Fed. Cir. 2001).

2. The Claimed Invention Was Made by Merck's Prior Art Vasotec Process.

As shown below on a limitation-by-limitation basis, Merck's use of the Vasotec Process in the early- and mid-1980s met each and every limitation of claims 16 and 17 of the '450 patent. Schwartz 270:5-9; 15-17. Dr. Schwartz's trial testimony on this contention was unrebutted.

- **16. A process for stabilizing an ACE inhibitor drug. . .**

As used in claim 16 (and 17), the term "a process for stabilizing" has been interpreted to mean "a method of making a pharmaceutical dosage form of an ACE inhibitor in which cyclization has been inhibited." Cl. Const. Order, at 2. Merck's Vasotec Process resulted in a formulation that was stable. Schwartz 268:3-6.

Vasotec obtained FDA approval. Brenner 134:19-22. Thus, this claim limitation is met by the Vasotec Process.[11]

- **. . . against cyclization . . .**

Because Vasotec was approved by the FDA, it was "stable" as this Court has interpreted that term, *i.e.*, cyclization was inhibited in the Vasotec Process to a sufficient extent so that it gained FDA approval. Cl. Const. Order, at 1; Schwartz 217:16-21.

- **. . . which comprises the step of contacting the drug with:**

As used in claim 16 (and 17), the term "the step of contacting the drug" has been interpreted to mean "mixing the components with one another." Cl. Const. Stip., at 4. The Vasotec Process included this mixing process. Schwartz 269:18-20. Accordingly, the Vasotec Process meets the contacting limitation of claims 16 and 17.

- **(a) a suitable amount of an alkali or alkaline earth-metal carbonate and,**

The Vasotec Process includes using sodium bicarbonate as a starting ingredient. DTX 174, at MCK 587. Sodium bicarbonate is an alkali metal

[11] Additionally, Merck's NDA confirms that during the manufacture of Vasotec, Merck utilized sodium bicarbonate in a wet granulation in order to create an alkaline environment. This environment facilitated a reaction in which the cyclization of enalapril was inhibited. DTX 174, at MCK 594-597; 627-628; 768-772. Such inhibition was sufficient to make a formulation that could garner FDA approval.

carbonate, and was included in Vasotec to inhibit cyclization. DTX 259, at TP 50711; DTX 38, at WL 30576; Schwartz 250:4-258:15. Vasotec was approved by the FDA for marketing. DTX 134, at MCK 16023; Brenner 134:4-25. Under the Court's claim construction, FDA approval means that a drug product is stable and specifically means that cyclization has been inhibited. Cl. Const. Order, at 1. Accordingly, the Vasotec process meets this claim limitation.

- **(b) one or more saccharides.**

As stipulated by the parties, lactose is a saccharide. Cl. Const. Stip., at 3. Therefore, since the Vasotec Process used lactose, it meets this limitation. DTX 117, at WL 74412; Schwartz 219:5-219:14.

- **17. The process of claim 16 wherein the drug is selected from the group consisting of quinapril, enalapril, and indolapril, or a pharmaceutically acceptable acid addition salt thereof**

The Vasotec Process included using enalapril maleate, a pharmaceutically acceptable acid addition salt of enalapril, as a starting ingredient of Vasotec. DTX 174, at MCK 587. Therefore all of the limitations of claim 17 are met by the Vasotec process.