therefore to establish conception. (Schwartz, Tr. 196:15-197:16, DTX 72). He even testified that conception might not have occurred until after the '450 patent issued in 1988 when FDA batch data was received. (Schwartz, Tr. 289:16-:25). Dr. Schwartz should have known his testimony on conception was improper, since he admitted that, in prior litigation, he had acknowledged that conception may occur before the invention is actually tested. (Schwartz, Tr. 285:12-287:23).

The defendant, Teva, bore the burden at trial of proving, by clear and convincing evidence, that the inventors failed to conceive the invention at the time they say they did. *Mahurkar*, 79 F.3d at 1578. For the foregoing reasons, Teva failed to meet this heavy burden.

B. ***Bohidar et al.* and *Shiromani et al.* Are Not Prior Art**

At trial, Teva relied on two publications, the *Bohidar et al.* paper (DTX 259) and the *Shiromani et al.* paper (DTX 38). These papers, however, are not prior art and have no bearing on the validity of the '450 patent.

As discussed above, the Warner-Lambert inventors conceived the '450 patent's claimed process of stabilizing quinapril against cyclization by August 1986. *Bohidar et al.* was not mailed to subscribers until September 9, 1986 (PTX 233), and Dr. Schwartz admitted that he could not testify when the article would have actually been received by those subscribers. (Schwartz, Tr. 351:11-:12). In fact, Dr. Schwartz testified that

he could not say that the *Bohidar et al.* paper (DTX 259) was publicly available any time before December 31, 1986. (Schwartz, Tr. 277:1-:4). Dr. Schwartz further admitted that the *Shiromani et al.* paper (DTX 38) was not publicly available any earlier than the *Bohidar et al.* paper. (Schwartz, Tr. 278:14-:22).

A publication is not considered publicly available for purposes of prior art consideration until it is actually received by the addressees. *Carella v. Starlight Archery & Pro Line Co.*, 804 F.2d 135, 139 (Fed. Cir. 1986). The evidence at trial showed that *Bohidar et al.* and *Shiromani et al.* could not have been publicly available any earlier than September 9, 1986.

Because, as discussed above, the inventors conceived the '450 invention before September 9, 1986, the *Bohidar et al.* paper (DTX 259) and the *Shiromani et al.* paper (DTX 38) are not, as a matter of law, prior art and thus have no bearing on patent validity. *See* 35 U.S.C. § 102(a) (to be prior art the printed publication must occur "before the invention thereof by the applicant for patent"); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986) (four articles, which the district court erroneously found to be of the utmost importance, were not prior art because they were dated after the conception of the patentee's invention).

At trial, Teva bore the burden of proving by clear and convincing evidence the status of these papers as prior art. *Mahurkar*, 79 F.3d at 1576 (The defendant "must persuade the trier of fact by clear and

convincing evidence that the Cook catalog was published prior to [the plaintiff's] invention date."). Teva failed to meet this burden.

C. There Is No Inequitable Conduct

1) Warner-Lambert did not withhold a known material reference

"Inequitable conduct resides in [the] failure to disclose material information, or submission of false material information, with an intent to deceive, and those two elements, materiality and intent, must be proven by clear and convincing evidence." *Kingsdown Med. Consultants, Ltd. v. Hollister Inc.*, 863 F.2d 867, 872 (Fed. Cir. 1988) (*en banc*). Proving intent to deceive means more than merely proving that the applicant intended to do what he did in patent prosecution. "[I]t means that the inventor intended to deceive or mislead the examiner into granting the patent." *Therma-Tru Corp. v. Peachtree Doors Inc.*, 44 F.3d 988, 995 (Fed. Cir. 1995). Information is "material" where "there is a substantial likelihood that a reasonable examiner would have considered the information important in deciding whether to allow the application to issue as a patent." *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1575 (Fed. Cir. 1996).

Where the charge of inequitable conduct is based on the alleged failure to disclose particular information, it is insufficient to prove "that art or information having some degree of materiality was not disclosed. To be guilty of inequitable conduct, one must have intended to act inequitably."

FMC Corp. v. Manitowoc Co., Inc., 835 F.2d 1411, 1415 (Fed. Cir. 1987). To prove that a party acted inequitably in failing to disclose information or a reference, "there must be clear and convincing evidence that the applicant made a deliberate decision to withhold a ***known*** material reference." *Baxter Int'l, Inc. v. McGaw, Inc.*, 149 F.3d 1321, 1329 (Fed. Cir. 1998) (emphasis added); *FMC Corp.*, 835 F.2d at 1415; *Univ. of Fla. Research Fndn., Inc. v. Orthovita, Inc.*, 1998 WL 54007129, *34 (N.D. Fla. 1998) (no inequitable conduct: "It is imperative that the applicant be shown to have known of the materiality of the undisclosed reference").

The Federal Circuit has strongly emphasized that intent is a separate element of an inequitable conduct defense and must be established by facts; even if a material reference was withheld, that fact alone is insufficient to establish intent. *Manville Sales Corp. v. Paramount Sys., Inc.*, 917 F.2d 544, 552 (Fed. Cir. 1990) ("However, materiality does not presume intent, which is a separate and essential component of inequitable conduct"); *Hebert v. Lisle Corp.*, 99 F.3d 1109, 1116 (Fed. Cir. 1996) ("Intent to deceive cannot be inferred solely from the fact that information was not disclosed; there must be a factual basis for a finding of deceptive intent."). Intent to deceive must be proven by clear and convincing evidence. *Kingsdown Med. Consultants, Ltd.*, 863 F.2d at 872.

(a) There is no clear and convincing evidence that the '450 inventors knew of the stabilizing function of sodium bicarbonate in Vasotec®

Today, Teva does not even assert that the Vasotec® formulation is material to claims 1-16 of the '450 patent -- and of course it is not. As discussed above, (pp. 49-53), it is now undisputed that Vasotec® does not employ a saccaride to inhibit hydrolysis or an ACE inhibitor that is susceptible to discoloration.

With respect to claims 16 and 17 (or original claims 18 and 19), carbonates (or alkali or alkaline earth metal salts) are only claimed insofar as they achieve stabilization of "an ACE inhibitor drug against cyclization." (PTX 1, claims 16 and 17; DTX 2, pp. 19-21). Accordingly, in order to prove the first prong of its inequitable conduct defense, under the *Baxter Int'l* line of cases discussed above, Teva needed to show by the very high burden of clear and convincing evidence that the '450 inventors ***knew*** that sodium bicarbonate stabilized against cyclization in the Vasotec® formulation. Indeed, Teva recognized this burden. In his opening, counsel for Teva promised this Court that "at least one of the inventors will testify before this Court that ***he knew*** that sodium bicarbonate was a stabilizer in Vasotec®." (Defendant's Opening Statement, Tr. 9).

Teva, however, never made good on its promise of showing that one of the inventors knew of the stabilizing function of sodium bicarbonate – and certainly did not establish this fact by clear and

convincing evidence. Indeed, we all know now that Merck took great pains to conceal this fact from competitors like Warner-Lambert, and felt that it had succeeded in concealing this fact as late as 1994. (*See* pp. 23-28).

As Dr. Schwartz conceded, cyclization is rare. (Schwartz, Tr. 294:22-295:2). In fact, in his long 35 year career in pharmaceutical formulation, Dr. Schwartz had never encountered a drug that cyclizes. (Schwartz, Tr. 294:17-:21). Nor had any of the Warner-Lambert inventors encountered cyclization prior to their development work on quinapril, or seen anything about it in the literature. (Harris, Tr. 44:25-46:2; Murthy, Tr. 512:13-:24). Accordingly, it is undisputed that the '450 inventors began their development efforts with a blank slate; with no knowledge of cyclization or any means to solve cyclization.

By the end of their quinapril development, the only information that the inventors had regarding the Vasotec® formulation was access to the tablets themselves, moisture absorption tests of the tablets, the package insert that discloses certain inactive ingredients and the knowledge that the sodium bicarbonate was included in the formulation and helped cause a pH of about 6.5 in the tablet. (Murthy, Tr. 533:18-534:8). With respect to the tablets themselves, it is undisputed that Warner-Lambert never attempted to reverse engineer the tablets (of course no one could), and therefore discerned nothing about the stabilization mechanism of Vasotec® from the tablets. (Murthy, Tr. 515:24-516:2). Teva has submitted no evidence that Warner-Lambert's moisture absorption tests could have identified any stabilizing

role for sodium bicarbonate, and in fact, these tests did not. (Murthy, Tr. 514:19-515:23). The package insert does not even disclose sodium bicarbonate and therefore provided no information on its possible role. (Murthy, Tr. 516:11-518:1).

Nor did the fact that sodium bicarbonate contributed to a pH of 6.5 in the Vasotec® tablets impart any knowledge that sodium bicarbonate was a stabilizer. Not knowing anything about cyclization, there would be no basis for concluding that "pH adjustment" underlies the stabilization of Vasotec® -- and in fact today, we know that pH adjustment is not the stabilization mechanism for Vasotec®. (Brenner, Tr. 599:16-600:23). Moreover, the pH-based experiment of Warner-Lambert as discussed above (pp. 6-12), failed to establish any connection between "pH adjustment" and the cyclization of quinapril either. (Harris, Tr. 56:14-23). Following that failed experiment with sodium bicarbonate and the possible role of pH in stabilizing quinapril, belief in pH as a stabilizing mechanism faded and was eventually "abandoned." (PTX 42, WL 029058: "Therefore, the use of buffers to control the pH of tablets was abandoned;" Harris, Tr. 56:2-13; Murthy, Tr. 529:2-:24). These failed pH-based experiments did not give the inventors any knowledge regarding either the stabilization mechanism of Vasotec®, or the role of sodium bicarbonate in that mechanism. (Harris, Tr. 58:2-60:5; Murthy, Tr. 526:11-:16).

Indeed, the inventor's failure when trying sodium bicarbonate is compelling evidence supporting the lack of any knowledge on the inventors'

part that sodium bicarbonate would be material. *Modine Mfg. Co. v. Allen Group Inc.*, 14 U.S.P.Q2d 1210, 1215-16 (N.D. Cal. 1989), *aff'd*, 917 F.2d 538 (Fed. Cir. 1990) (no inequitable conduct despite admitted materiality of withheld prior art since, *inter alia*, inventor believed the subject prior art would not work in his invention); *see also Allen Archery Inc. v. Browning Mfg. Co.*, 819 F.2d 1087, 1093-94 (Fed. Cir. 1987) (inventor's failure to disclose reference that he considered "radically different" from his claims establishes that the nondisclosure was not intentional ***regardless*** of whether or not the reference is material); *FMC Corp.*, 835 F.2d at 1416 (no inequitable conduct since "the applicant had no knowledge of materiality" of the prior art).

The paper, *Bohidar et al.,* could not have told Warner-Lambert anything regarding the role of sodium bicarbonate in Vasotec® when they were involved in their development work, because it did not exist publicly at that time. It only became publicly available after the invention date of the '450 patent; therefore, it was not prior art as discussed above (pp. 33-35). The inventors correctly did not consider it prior art that could be relevant to their invention. (Harris, Tr. 535:2-:21). Moreover, we know today that Merck apparently concealed (or deleted) the identity of the drug at issue in *Bohidar et al*, as part of its strategy to conceal its stabilization process and

the role of sodium bicarbonate in that process. (Brenner, Tr. 162:25-163:20).[10]

It is clear that following the inventors' development work on quinapril, they still had no knowledge that sodium bicarbonate was a stabilizer of Vasotec®. In a December 19, 1986 memorandum, when asked by his supervisor to ***review the literature*** and identify the excipients recognized and accepted as diluents, as possible alternatives to magnesium carbonate, Murthy mentions sodium bicarbonate among several possibilities, and mentions several known uses for sodium bicarbonate, ***but never even hints that*** sodium bicarbonate could stabilize an ACE inhibitor. (DTX 287). This omission is compelling evidence that the inventors simply did not possess the knowledge that Teva attributes to them, as Dr. Murthy testified:

> Q: And if you knew sodium bicarbonate stabilized an ACE inhibitor, that would have been a pretty important thing to tell Dr. Braun when he's looking for alternative excipients, right?
>
> A: Yes.
>
> Q: And you didn't know that in December 1986; correct?

[10] Dr. Murthy testified that today, in hindsight, he sees the "possibility" that Bohidar discloses a stabilizing role for sodium bicarbonate in enalapril. This "possibility," however, does not meet the required standard of knowing that sodium bicarbonate is a stabilizer, and there is no evidence that Dr. Murthy recognized this "possibility" back when he first read the reference, months after his development work was complete. (Murthy, Tr. 536:13-:17).

A: Yes, that is correct.

(Murthy, Tr. 532:9-533:5).

(b) Dr. Schwartz's analysis lacks credibility

Given their failure to prove that Warner-Lambert ***knew of*** the stabilizing function of sodium bicarbonate in Vasotec®, Teva likely will try to rely on Dr. Schwartz's testimony to assert that Warner-Lambert "should have known" this information. Specifically, even though he knew in 1994 that Merck was still concealing its stabilization mechanism for Vasotec®, Dr. Schwartz testified at trial that one of ordinary skill in 1986 would have been able to easily discern Merck's secret stabilization mechanism. (Schwartz, Tr. 328:3-:10). However, many of the assertions Dr. Schwartz made in the course of his testimony were clearly either misinformed or misleading.

Although Dr. Schwartz is no doubt a qualified pharmacist, he lacks the credentials to testify, as he did, about degradation pathways, and complex chemical analyses available to analyze those pathways. Indeed, Dr. Schwartz conceded that, in his career, he has not "dealt with" degradation pathways on a regular basis. (Schwartz, Tr. 292:10-:13). In fact, at one point in the litigation, he approached a colleague, Dr. Gennaro, an analytical chemist, to get involved in the case based on his belief that Dr. Gennaro would be more familiar than him with the study of degradation pathways and "degradation mechanism(s)." (Schwartz, Tr. 292:14-:24). Dr. Gennaro

did become an expert for Teva, but was unable to continue his duties due to illness.

The thrust of Dr. Schwartz's opinion is that, knowing the list of starting ingredients in the Vasotec® formulation, one of ordinary skill would know sodium bicarbonate was a stabilizer since (i) the stabilizer must be one of the ingredients in the formulation, (ii) it is not possible that sodium bicarbonate was performing any non-stabilizing role in Vasotec®, and (iii) because sodium bicarbonate was a known stabilizer in this time period, by process of elimination, it must therefore be the stabilizer. From that point in his "analysis," Dr. Schwartz asserted that (iv) by "reverse engineering" the tablets, one could determine that a chemical reaction occurred during wet granulation and (v) by testing pH of the Vasotec® tablets, one could determine the extent of the reaction. On cross-examination, however, each of these opinions was shown to be wrong for at least the following reasons:

i. It is not true that one of the ingredients of the Vasotec® formulation is necessarily the stabilizer

As Dr. Schwartz fully knows, even if one of ordinary skill knew that enalapril degraded via cyclization, it is simply not true that the stabilizer would necessarily be found in the list of excipients included in the formulation. (Schwartz, Tr. 310:6-:16). Indeed, as Dr. Schwartz conceded on cross-examination, the Vasotec® formulation could have been stabilized – not by addition of a stabilizer – but by proper packaging, by deletion of a

destabilizing excipient, or by the choice of particular processing conditions, such as by dry blending to eliminate moisture. (Schwartz, Tr. 309:5-:13). In fact, Dr. Schwartz conceded that one of the ways Merck stabilized Vasotec® was by elimination of the de-stabilizing excipient microcrystalline cellulose. (Schwartz, Tr. 310:17-:21). Accordingly, in 1986, one of ordinary skill could have easily concluded ***none*** of the excipients in the Vasotec® formulation is the stabilizer of the formulation.

ii. Dr. Schwartz knows fully well that sodium bicarbonate can – and does – perform a common function in the Vasotec® formulation besides stabilizer

In the next step of Dr. Schwartz's "analysis," he attempted to articulate all of the common uses for sodium bicarbonate and then argue that, since sodium bicarbonate could not be serving any of these common functions in the formulation, it must be a stabilizer. (Schwartz, Tr. 242:20-247:1). But Dr. Schwartz apparently forgot one common function. On cross examination, when asked whether sodium bicarbonate could be functioning as a disintegrant in the formulation, Dr. Schwartz essentially said that this was not technically possible; it did not "make sense." (Schwartz, Tr. 312:20-313:10). Dr. Schwartz apparently did not recall, though he did ultimately admit, that in a sworn affidavit in 1994, he had stated that sodium bicarbonate did, in fact, perform the common function of disintegrant in the

Vasotec® formulation. (Schwartz, Tr. 312:14-313:23). His initial opinion to the contrary was either misinformed or misleading.

iii. Sodium bicarbonate was not a known stabilizer in 1987

Dr. Schwartz's testimony that sodium bicarbonate was a known stabilizer in 1987 was completely without support, and was contradicted by his prior testimony in this case. First, prior to this litigation, Dr. Schwartz was not aware of ***any*** discussions in the literature in 1986 of ***any*** drug that cyclizes, or any specific means whatsoever of stabilizing against cyclization. (Schwartz, Tr. 295:21-296:3). He could not, therefore, know of any use of sodium bicarbonate as a stabilizer against cyclization. Second, Dr. Schwartz gave absolutely no examples of use of sodium bicarbonate as a known stabilizer, and conceded on cross-examination that he could not give a single example of sodium bicarbonate being used prior to 1987 to stabilize ***any*** tablet formulation against ***any*** degradation pathway. (Schwartz, Tr. 303:13-:17, 306:18-307:21). On the contrary, Dr. Schwartz admitted on cross-examination that he now realizes, based on materials cited by Warner-Lambert experts, that in 1986, bicarbonates and carbonates were understood to actually promote degradation via cyclization in certain antibiotics. (Schwartz, Tr. 305:10-:18).

Indeed, Dr. Schwartz's unsupported assertions were a dramatic departure from his deposition testimony, in which he had conceded that, by looking at these same ingredients, one would have "at best a mere suspicion"

that sodium bicarbonate was a stabilizer. (Schwartz, Tr. 320:23-321:4; *Summary Judgment Opinion*, PTX 235, p. 26: "Dr. Schwartz conceded that --- just looking at the listing of ingredients, [he] would not know that sodium bicarbonate has ***any*** role in stabilizing enalapril.")

iv. One cannot reverse engineer the Vasotec® tablets to determine that a chemical reaction occurred

Dr. Schwartz began this "analysis" by suggesting that as a matter of "elementary chemistry," knowing that Vasotec® was formulated via wet granulation would suggest that a chemical reaction occurred in the wet granulation between sodium bicarbonate and enalapril maleate. (Schwartz, Tr. 246:9-:13). However, this assertion is belied by Dr. Schwartz's testimony in the Canadian litigation. Even when Merck told him that sodium bicarbonate was a stabilizer in that litigation, Dr. Schwartz was still unwilling to offer an opinion that a reaction took place between the enalapril maleate and the sodium bicarbonate. (Schwartz, Tr. 323:7-:16). Moreover, Dr. Schwartz's testimony that he could, by chemical analyses, "reverse engineer" the tablets and determine that enalapril maleate had converted to enalapril sodium by measuring "the sodium on the [sic] enalapril maleate sodium," was simply specious. (Schwartz, Tr. 232:11-:19). First, Dr. Schwartz conceded that these analyses he was positing were properly in the area of expertise of a chemist, not a pharmacist like him. (Schwartz, Tr. 317:17-:19). And, Dr. Schwartz also conceded that he has

never attempted to reverse engineer a tablet in his life. (Schwartz, Tr. 318:3-:6, 351:13-17). Indeed, when confronted with the actual composition of the Vasotec® tablets versus the starting ingredients, Dr. Schwartz sheepishly admitted that he could no longer say for sure that reverse engineering was even possible. (Schwartz, Tr. 316:23-317:10). He also admitted – in contradiction to his direct testimony – that in reality he did not know of any test that would allow him to differentiate between enalapril maleate and the stabilized reaction product, enalapril sodium. (Schwartz, Tr. 318:7-:15).

v. One cannot determine the extent of reaction from pH

Knowing from Dr. Brenner's testimony in this case that the extent of reaction is key to the stabilization process of Vasotec®, Dr. Schwartz evidently felt compelled to offer an opinion that extent of reaction can also be "reverse engineered" from the tablet by measuring the tablet's pH. (Schwartz, Tr. 246:24-247:22). This assertion was either misleading or misinformed. As Dr. Schwartz conceded, "Dr. Brenner has far more background and experience with the chemistry underlying the chemical stabilization of ACE inhibitors" than he does. (Schwartz, Tr. 299:9-:15). In direct contradiction to Dr. Schwartz's testimony, Dr. Brenner explained that by "measuring the pH, you get no useful information about the extent of reaction." (Brenner, Tr. 622:21-:22). Accordingly, Merck needed to develop a separate non-pH related proprietary test to determine extent of reaction. (Brenner, Tr. 621:4-623:14). No one of ordinary skill in 1986

outside Merck would be able, therefore, to reverse engineer the extent of reaction from the Vasotec® tablets.

In sum, the extent to which Dr. Schwartz had to rely on opinions that were either misleading or misinformed to support his speculative thesis that one of ordinary skill in 1986 could have determined the stabilization process of Merck's Vasotec® tablets, highlights that Merck was justified in their conclusion that this information could not be determined at the time. There can be no intent to deceive in not disclosing that which was neither known nor knowable. *Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 288 F.Supp.2d. 601, 632-33 (D. Del. 2003) (Teva's inequitable conduct defense rejected despite the materiality of the withheld information, since the patentee was not shown to have known the relevance of the information in his possession).

Nor has Teva pointed to any direct evidence, much less clear and convincing evidence, of any intention to deceive – because no such evidence exists. As Dr. Murthy explained, there could be no plausible reason why he, or the other inventors, would have any motivation to deceive the Patent Office. Indeed, to believe that they did, one would have to believe that these inventors conspired to hide the little information they knew about Vasotec®, and thereby put their valid invention at risk, all for the purpose of obtaining just two additional and important claims at the back end of their patent. Not only is there no evidence that this occurred, the very suggestion defies common sense.

2) The Vasotec® information was not highly material

(a) European prosecution history

A careful examination of the European prosecution history of the '450 patent demonstrates that the Vasotec® formulation was not material,[11] and buttresses the conclusion that one of ordinary skill -- including Dr. Murthy -- would not be able to discern any stabilizing role for sodium bicarbonate in this formulation. Below, side-by-side, is original filed claim 18 of the '450 patent application, issued claim 16 of the '450 patent and issued claim 12 of the European '450 equivalent:

Originally filed Claim 18 of the '450 Patent Application (DTX 2, 21)	**Issued Claim 16 of the '450 Patent (PTX 1)**	**Issued Claim 12 of European Patent 280999 (equivalent to the '450 patent) (PTX 110, TP 19583)**
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.	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 carbonate and, (b) one or more saccharides.	A process for stabilizing an ACE inhibitor ***drug as defined in claim 1*** 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.

As can be seen, the claims are nearly identical. During the summary judgment proceedings, however, Teva attempted to confuse the

[11] *See* Trial Tr. 17:14–25:12 and Plaintiff's Demonstratives PD 35-53, 91 and 94 for a detailed step-by-step explanation of the European prosecution history.

issue, suggesting that European claim 12 is narrower than the U.S. '450 filed or issued claims by virtue of the "***drug as defined in claim 1***" language. Specifically, Teva suggested that this language reflects an incorporation of the disclaimer of the Vasotec® formulation contained in European claim 1. This clearly is not so, however.

In fact, the Vasotec® formulation, which was before the European Examiner (in the form of Dictionnaire Vidal), was never cited or even discussed as relevant against claim 12, and the "drug as defined in claim 1" language was added to address a concern of the European Examiner totally unrelated to Vasotec®. Specifically, on February 28, 1991, ***eight months*** before the discussions between Warner-Lambert and the European Examiner regarding "the problem of novelty with respect to document Dictionnaire Vidal 1985," the European Examiner indicated that he only had one remaining objection with respect to claim 12 (then-numbered claim 14):

> 14. 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.

(PTX 110, TP 19567). Significantly, at this same time, again long before Dictionnaire Vidal was substantively discussed, claim 15, which specifically claims, *inter alia*, a process of stabilizing enalapril against cyclization by

contacting it with, sodium bicarbonate, was judged by the Patent Examiner to be "allowable" over the prior art, including Dictionnaire Vidal. (PTX 110, TP 19570).

The objection to claim 14 had nothing to do with novelty, obviousness or Dictionnaire Vidal; instead, the European Examiner was concerned that the term "ACE inhibitor drug" was too broad, in that Warner-Lambert had not shown its invention to work, in the European Examiner's view, for all ACE inhibitors beyond the "specific group" taught in the specification of the patent, *i.e.*, "quinapril and structurally-related drugs, which are susceptible to certain types of degradation through cyclization via internal nucleophilic attack, hydrolysis or oxidation." (*See* PTX 110, TP 19570 and point 3 on TP 19552).

The language "drug as defined in claim 1" therefore was added to issued European claim 12 -- not because of any need to address or disclaim the Vasotec® formulation -- but merely to restrict the definition of the ACE inhibitors covered by this claim to those specifically covered by the chemical structure shown in paragraph 1(a) of issued claim 1. (PTX 110, TP 19561). Enalapril was not disclaimed, the enalapril composition was not disclaimed and the Dictionnaire Vidal disclosure of the enalapril formulation was not cited against, or even discussed with respect to claim 12. Indeed, the fact that European claim 12, and the drug defined in claim 1, still covers enalapril is indisputable from examination of issued European claim 13,

which specifically identifies enalapril as among the class of ACE inhibitors included in the group of claim 12. (PTX 110, TP 19579).

Accordingly, it is absolutely clear that a claim even broader in scope than '450 issued claim 16, and equal in scope to original '450 claim 18, was allowed over the Vasotec® formulation. And contrary to this Court's summary judgment opinion (*Summary Judgment Opinion*, PTX 235, p. 38), absolutely ***no*** attention was "paid to the Merck product" with respect to this claim.

There can only be one rational explanation for this history: like Dr. Murthy and like Teva's expert Dr. Schwartz, knowing only that Vasotec® contains sodium bicarbonate, the European Examiner could discern nothing that would lead him to conclude that sodium bicarbonate stabilizes against cyclization in this formulation. If the formulation did suggest a stabilizing role for sodium bicarbonate in Vasotec®, then European claim 12, which literally covers a process for stabilizing enalapril against cyclization, comprising the step of contacting enalapril with sodium bicarbonate and a saccharide, logically could not have been allowed. Indeed, as observed by this Court (*Summary Judgment Opinion*, PTX 235, p. 37), the European Examiner was explicit in noting the failure of the Vasotec® formulation to provide this teaching:

> "The examining division agrees with the Applicant that ***there is no teaching in the prior art to use the combination of an alkali or alkaline earth metal carbonate and the saccharide to stabilize an ACE***

inhibitor as claimed in claim 1. The newly submitted claims, however, are directed to the compositions are such and not to the use of them for said purpose." (emphasis added).

(b) Vasotec® does not affect the validity of original filed claims 18 and 19

This Court's preliminary materiality finding, *i.e.*, that "Vasotec® anticipated two of the claims [filed claims 18 and 19] set forth in Warner-Lambert's original application that led to issuance of the '450 patent," is not correct. These claims are process claims. As discussed below (with respect to the almost identical issued claims 16 and 17), these process claims are not anticipated by Vasotec® because insufficient information regarding Merck's Vasotec® process was available in the prior art to place Merck's process in the public domain. Indeed, Merck deliberately concealed its process, which as explained below, disqualifies it as prior art.

D. Claims 16 And 17 Of The '450 Patent Are Valid

By statute, the '450 patent is entitled to a presumption that it is valid. 35 U.S.C. § 282; *Datascope Corp. v. SMEC, Inc.*, 776 F.2d 320, 323 (Fed. Cir. 1985). The defendant, Teva, bears the burden of proving that the patent is invalid by clear and convincing evidence. This heavy burden of proof is "constant" and "never changing," and applies to every possible basis for challenging the '450 patent's validity. *American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350, 1360 (Fed. Cir. 1984); *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1570 (Fed. Cir. 1987).

1) Teva failed to prove that Claims 16 and 17 are anticipated by the Merck Vasotec® process because the Merck process was not publicly available

(a) Applicable legal standards

A fundamental policy of the patent laws is to encourage placing the public in possession of an invention through early, full disclosure of the elements of the invention:

> "Early public disclosure is a linchpin of the patent system. As between a prior inventor who benefits from a process by selling its product but suppresses, conceals, or otherwise keeps the process from the public, and a later inventor who promptly files a patent application from which the public will gain a disclosure of the process, ***the law favors the latter.***"

W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1550 (Fed. Cir. 1983) (emphasis added).

At trial, Teva argued that claims 16 and 17 of the '450 patent are anticipated under 35 U.S.C. § 102(g) by the Merck "Vasotec® process" (*see* Trial Tr. 11:14-:25). The defendant must prove anticipation by clear and convincing evidence. *PIN/NIP, Inc. v. Platte Chem. Co.*, 304 F.3d 1235, 1243 (Fed. Cir. 2002).

Section 102(g) bars a patent to a person if:

> ***before such person's invention thereof***, the invention was made in this country by another inventor ***who had not abandoned, suppressed, or concealed it.***"

35 U.S.C. § 102(g)(2) (emphasis added).

By its plain terms, for § 102(g) to apply, Teva must prove that, before Warner-Lambert's invention of the '450 patent, Merck had not suppressed or concealed its Vasotec® process. *See, e.g., Palmer v. Dudzik*, 481 F.2d 1377, 1385 (C.C.P.A. 1973); *Paulik v. Rizkalla*, 760 F.2d 1270, 1273-75 (Fed. Cir. 1985) ("in each case where the court deprived the de facto first inventor of the right to the patent, the second inventor had entered the field during a period of either inactivity or ***deliberate concealment*** by the first inventor") (emphasis added).

In *Palmer v. Dudzik*, Palmer had made his invention in the Fall of 1965 which was some two years before Dudzik conceived that same invention. 481 F.2d at 1379-80. Nonetheless, Palmer's prior invention was not a bar to Dudzik's later patent on that invention under 35 U.S.C. § 102(g) because the court found that Palmer had intentionally suppressed and concealed the invention before Dudzik's invention thereof. *Id.* at 1385. Indeed, Palmer's prior invention was not considered prior art even though he had decided to make public his invention ***after*** Dudzik's conception by filing for a patent application. *Id.* at 1380. In addition, the court found that Palmer's commercialization of a product made by the concealed process was not a public disclosure of the process itself. *Id.* at 1386.[12]

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[12] 35 U.S.C. § 102(g) usually arises in *inter parties* interference proceedings in the PTO. The legal standards under § 102(g) in these cases generally apply in district court litigations, except that the defendant in a

(continued . . .)

At trial, counsel for Teva erroneously claimed that "[a]ll you have to show is a process was actually done in the prior art. It doesn't matter if the process was secret or not." (Trial Tr. 239:14-:20.) This assertion is squarely contradicted by the plain language of 35 U.S.C. § 102(g) and the Federal Circuit case law discussed above. *See also Oddzon Prods., Inc. v. Just Toys, Inc.*, 122 F.3d 1396, 1402 (Fed. Cir. 1997) (Section 102(g) "relate[s] to knowledge manifested by acts that are essentially public.").

At trial, Teva counsel also cited *Dow Chem. Co. v. Astro-Valcour, Inc.*, 267 F.3d 1334 (Fed. Cir. 2001), but this case does not support Teva's argument and is inapplicable on its facts. Unlike the '450 patent-in-suit, the patent in *Dow* was for a product, not for a process. 267 F.3d at 1339 n.4 & 1342 ("we treat the invention as being a single invention, *i.e.*, the foam"). Contrary to Teva's argument at trial, the Federal Circuit there specifically found that the defendant had made a public disclosure of that product. *Id.* at 1343 ("Here, AVI's public disclosure of its isobutene-blown foam invention occurred through commercialization of it's foam."). Moreover, *Dow* expressly did not involve deliberate concealment, like Merck's, but rather the different issue of whether an alleged short delay

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(continued-)

litigation bears a heavier burden of proving a prior invention, *i.e.*, by clear and convincing evidence, since an issued patent is being challenged. *See Environ Prods., Inc. v. Furon Co.*, 215 F.3d 1261, 1265 (Fed. Cir. 2000).

between the invention of the product, and the public disclosure of that product, was so unreasonable in itself as to raise an inference of concealment. *Id.* at 1342.

(b) Before Warner-Lambert's invention of the '450 patent, Merck had suppressed and concealed its Vasotec® process

Claims 16 and 17 of the '450 patent are to a process, not to a product. Teva's own expert has agreed that in order to demonstrate anticipation it is necessary to show that one of ordinary skill could have discerned that sodium bicarbonate is stabilizing enalapril maleate against cyclization. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1574 (Fed. Cir. 1986) ("anticipation requires the disclosure in a prior art reference of each and every element as set forth in the claim").

As discussed above, the evidence at trial showed that Warner-Lambert conceived its invention by August 1986. (*See* pp. 12-15, above). The evidence at trial further showed that, before Warner-Lambert's invention in August 1986, Merck had made a deliberate decision to forego filing for a patent and, instead, conceal as a trade secret its process for stabilizing Vasotec® using sodium bicarbonate ("the Vasotec® process") (*see* pp. 23-28, above). Dr. Brenner specifically testified that Merck was able to maintain its Vasotec® process as a trade secret at least to the late 1980s or early 1990s. (Brenner, Tr. 156:10-:14, 601:22-602:1). He confirmed that, prior to 1987, Merck never disclosed in any publicly

available form its process for stabilizing Vasotec®. (Brenner, Tr. 154:12-:15). Merck, in fact, continued its efforts to conceal its Vasotec® process from the public in its 1994 Canadian litigation with Apotex (*see* pp. 26-28, above).

At trial, Teva offered no evidence, let alone clear and convincing evidence, to refute Dr. Brenner's testimony. Instead, Teva attempted sleight-of-hand by deliberately confusing irrelevant confidential internal Merck information and irrelevant public knowledge in the 1990s and today, none of which is prior art, with the state of the prior art in 1986 at the time of Warner-Lambert's invention.

For example, Teva attempted to use a declaration which Dr. Brenner had prepared in 1999, some thirteen years after the relevant time period. That declaration, however, nowhere says that any information about the Vasotec® process was in the public domain by 1986 or at any time in the late 1980s. (DTX 301; Brenner, Tr. 137:9-:20).[13]

Teva also relied at trial on the Merck NDA. Dr. Schwartz admitted, however, that the NDA is confidential (Schwartz, Tr. 354:3-:4). And, in response to questioning from the Court, Teva conceded through

[13] The first reference in the declaration to any public knowledge is in paragraph 5 discussing public testimony given in 1994, eight years after the '450 invention, by a Merck marketing vice-president in Canadian litigation. And, even as to that irrelevant 1994 Canadian testimony, Merck was said in paragraph 5 of the declaration to have generically referred only to addition of a "stabilizer," thus continuing the concealment of the identity of that stabilizer. (*See* DTX 301; Schwartz, Tr. 325:2-:9, 326:24-327:1).

counsel that the Merck NDA was not in the public domain. (Trial, Tr. 214:7-:10). "Insider knowledge," as this Court recognized in its October 2, 2003 summary judgment ruling, cannot be attributed to the public at large. *See Summary Judgment Opinion*, PTX 235, p. 27, *citing Oddzon Prods., Inc. v. Just Toys, Inc.*, 122 F.3d 1396, 1402 (Fed. Cir. 1997) ("Thus, the patent laws have not generally recognized as prior art that which is not accessible to the public.").

Teva also relied on the Vasotec® tablets and the listing of ingredients found in the package insert and Dictionnaire Vidal. These, of course, are not the Vasotec® process. They do not describe a process of stabilizing enalapril against cyclization or the role of sodium bicarbonate in the Vasotec® formulation. In *W.L. Gore*, the Federal Circuit made clear that disclosure of a prior art ***product*** cannot anticipate a later patent to a ***process***, unless the public could have learned the patented process simply by examining the earlier product. *W.L. Gore*, 721 F.2d at 1550 ("There is no reason or statutory basis, however, on which [a third-party's] secret commercialization of a process, if established, could be held a bar to the grant of a patent to [the plaintiff] on that process."); *Fromson v. Citiplate, Inc.*, 886 F.2d 1300, 1302 (Fed. Cir. 1989), *aff'g*, 699 F. Supp. 398, 400 (E.D.N.Y. 1988) (sale of a printing plate did not disclose the process by which it was formed); *Oddzon*, 122 F.3d at 1402.

As discussed above (pp. 23-28), Merck was aware of the Vasotec® tablets, the package insert and the Dictionnaire Vidal when it

decided to maintain as a trade secret its process for stabilizing enalapril and the role of sodium bicarbonate in that process, and the consensus at Merck was that those of ordinary skill in the art could not discern the process from these sources. (Brenner, Tr. 157:12-158:20, 160:25-162:7).

Faced with a lack of any evidence of public disclosure of the Vasotec® process before August 1986, Teva attempted to have Dr. Schwartz testify that the tablets and listing of ingredients could have been "reverse engineered" to figure out the Vasotec® process. On cross-examination, however, Dr. Schwartz's speculative, hindsight testimony fell apart. (*See* pp. 46-47, above).

The prosecution of Warner-Lambert's European counterpart to the '450 patent confirms that the mere knowledge of the Vasotec® ingredients would have disclosed nothing to one of skill in the art about the process for stabilizing enalapril. As discussed above, a process claim even broader in scope than '450 issued claim 16, and equal in scope to original '450 claim 18, was allowed over the Vasotec® tablets. As observed by this Court in its October 2, 2003 summary judgment opinion (PTX 235, p. 37), the European Examiner explicitly noted the failure of the Vasotec® formulation information, including Dictionnaire Vidal, to teach the process by which the enalapril is stabilized against cyclization: "The examining division agrees with the Applicant that there is no teaching in the prior art to use the combination of an alkali or alkaline earth metal carbonate and the

saccharide to stabilize an ACE inhibitor as claimed in claim 1." (*See* pp. 49-53, above).[14]

Finally, Teva relied on the *Bohidar et al.* and *Shiromani et al.* papers (DTX 259 and DTX 38) as alleged public disclosures of the Vasotec® process. But, as discussed above, these papers are not prior art since they were published after the conception of the '450 patented invention. As a result, even if, as Teva alleged, Merck had stopped concealing the Vasotec® process and made certain aspects public at the time of these papers, § 102(g) would still not apply -- the alleged public disclosure had not been before the '450 patented invention in August 1986. *See* 35 U.S.C. § 102(g); *Palmer*, 481 F.2d at 1385; *Paulik*, 760 F.2d at 1273-75. The papers are therefore irrelevant to the validity of the '450 patent and it is error to rely upon them. (*See* pp. 33-35, above).

Moreover, even were they prior art, which they are not, Teva failed to provide clear and convincing evidence that these papers do in fact

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[14] In the October 2, 2003 summary judgment opinion, the court commented that "it would hardly require one skilled in the art to conclude that the [Vasotec] product was derived from 'contacting' its various ingredients with each other." Claim 16 of the '450 patent, however, requires more than that the product be manufactured by contacting its ingredients with each other. It requires a process for stabilizing an ACE inhibitor against cyclization using an alkali or alkaline earth metal carbonate. As discussed above, Merck did not make public that process before the invention of the '450 patent. Moreover, as discussed above (pp. 20-23), simply contacting enalapril with sodium bicarbonate would not stabilize enalapril against cyclization as required by Claim 16.

disclose the Vasotec® process. Dr. Schwartz admitted that the *Bohidar et al.* paper fails to identify the drug being discussed. (Schwartz, Tr. 352:2-:4). Dr. Schwartz also admitted that the *Shiromani et al.* paper makes no mention of the use of sodium bicarbonate. (Schwartz, Tr. 352:5-:7). Dr. Schwartz further agreed with Dr. Brenner that the authors of the *Bohidar et al.* paper were known to have been primarily working on a different ACE inhibitor, lisinopril. (Brenner, Tr. 153:12-154:4; Schwartz, Tr. 330:11-333:10). Dr. Schwartz agreed that the failure to identify enalapril in the *Bohidar et al.* paper makes sense if Merck was trying to keep the stabilization process a trade secret. (Schwartz, Tr. 334:13-:17).

Dr. Brenner testified that Merck was aware of the *Bohidar et al.* paper when it decided to maintain as a trade secret its process and the role of sodium bicarbonate in that process, and the consensus at Merck was that those of ordinary skill in the art could not make a stable tablet even with the information in the Vasotec® tablets, the package insert, the Dictionnaire Vidal and *Bohidar et al.* (Brenner, Tr. 162:11-163:20, 164:19-165:24). In fact, Dr. Brenner testified that the failure to identify the drug in the *Bohidar et al.* paper was "part of the strategy to minimize the information in the article so as not to be helpful." (Brenner, Tr. 163:7-:11).

In sum, before the invention of the '450 patent, the Merck Vasotec® process had been deliberately suppressed and concealed. One of ordinary skill in the art, in August 1986, would not have had any reason to know that sodium bicarbonate was used in the process of stabilizing

enalapril, and actually might have believed that sodium bicarbonate could generally cause degradation through cyclization. Teva has failed to prove by clear and convincing evidence that, before the invention of the '450 patent, Merck had not suppressed or concealed its Vasotec® process. Accordingly, Teva has failed to prove that claims 16 and 17 are invalid under 35 U.S.C. § 102(g).

2) The available Vasotec® information did not enable the practice of claims 16 and 17 of the '450 patent

In addition to failing to prove that the Vasotec® process was disclosed in the prior art, Teva also failed to prove that the publicly available information at the time of the '450 invention would have enabled one of ordinary skill in the art to practice a process of stabilizing an ACE inhibitor against cyclization using an alkali or alkaline earth metal carbonate.

(a) Applicable legal standards

In order for a patent claim to be invalid over the prior art, that prior art must enable the patented invention, thus placing the allegedly disclosed matter in the possession of the public. To the extent a defendant is relying on a single reference to argue anticipation, that reference must itself be enabling. *Elan Pharmaceuticals, Inc. v. Mayo Found. for Med. Educ. and Res.*, 346 F.3d 1051, 1054 (Fed. Cir. 2003); *Akzo N.V. v. United States Int'l Trade Comm'n*, 808 F.2d 1471, 1479 (Fed. Cir. 1986). And, to the extent the defendant is relying on multiple references to argue obviousness under 35 U.S.C. § 103, the totality of the teachings in the references must be

enabling. *Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551 (Fed. Cir. 1989) ("In order to render a claimed ... method obvious, the prior art must enable one skilled in the art to make and use the ... method."); *Rockwell Int'l Corp. v. United States*, 147 F.3d 1358, 1365 (Fed. Cir. 1998) ("The prior art must be enabling.").

To be enabling, the prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation. *Elan*, 346 F.3d at 1054. The defendant bears the burden of proving by clear and convincing evidence that a prior art reference is enabling. *Abbott Labs. v. Diamedix Corp.*, 969 F. Supp. 1064, 1067-68 (N.D. Ill. 1997); *see Mahurkar*, 79 F.3d at 1576.

Courts will therefore uphold patent validity where the defendant fails to prove, by clear and convincing evidence, that the prior art enabled one of skill in the art to practice the patented invention. *See In re Hoeksema*, 399 F.2d 269, 275 (C.C.P.A. 1968) (prior art reference disclosing a chemical compound did not render obvious a later patent application claiming that same compound, where the prior art reference failed to contain an enabling disclosure of a process for making the compound); *In re LeGrice*, 301 F.2d 929, 936, 944 (C.C.P.A. 1962) (publication showing the identical roses sought to be later patented was not an anticipation where it did not actually enable one of skill in the art to produce the disclosed roses); *Reading & Bates Construction Co. v. Baker Energy Resources Corp.*, 748 F.2d 645, 651-52 (Fed. Cir. 1984) (no anticipation where brochure boasting

the ability and results of a patented process did not enable the performance of that process); *Akzo*, 808 F.2d at 1479 (no anticipation where prior art patent failed to enable one of skill in the art to make the claimed aramid fibers); *Rockwell*, 147 F.3d at 1365 (defendant failed to show any prior art that taught with a reasonable likelihood of success how to grow a single specific crystal film on a substrate using a certain reagent).

(b) The available Vasotec® information did not enable the practice of a process for stabilizing an ACE inhibitor against cyclization

Teva failed to prove by clear and convincing evidence that the mere disclosure of the Vasotec® information would have enabled one of skill in the art in 1986 to practice a process of stabilizing enalapril against cyclization using sodium bicarbonate.

As discussed above, Dr. Brenner explained how the process of stabilizing enalapril against cyclization used internally at Merck was complex and unpredictable. (*See* pp. 20-21). The stabilization depended on the extent to which an *in-situ* deprotonation reaction between enalapril maleate and sodium bicarbonate went to completion in the limited water of wet granulation. The reaction depended on ensuring that numerous factors were carefully controlled, including an unusually high temperature for mixing, at least a two-to-one ratio of sodium bicarbonate to enalapril, a high-shear mixing method, a long duration of mixing, a certain holding time in

the mixer before drying, and the particle size of the sodium bicarbonate.[15] To analyze the extent of the reaction, Merck had to use a special analytical test that it developed and maintained internally. Merck devoted considerable manpower and two to three years of experimentation in order to devise its process, which it never publicly revealed before the invention of the '450 patent. (*See* pp. 23-28, above). Dr. Schwartz admitted that, during the Canadian litigation, he had seen Merck report after Merck report reflecting a "great deal of experimentation." (Schwartz, Tr. 300:17-:22, 302:9-:12). Indeed, as Dr. Brenner put it, the enalapril project was the most difficult of all the formulation projects he worked on during his 25 years at Merck. (Brenner, Tr. 616:4-:17).

Nor was any guidance readily available in the public art. Again, as discussed above, degradation of a drug via cyclization was rare in the 1986 time frame. And with respect to the only classes of drugs generally known to cyclize in that time period, carbonates and bicarbonates were believed to promote degradation, not prevent it. None of the prior art provided any teaching of the critical factors used by Merck necessary to achieve stabilization of enalapril using sodium bicarbonate. (*See* pp. 20-23, above). Instead, as Dr. Brenner explained, one of skill would have tried to

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[15] In contrast to Merck's experience, the process of the '450 patent invention did not involve reacting any excipients with quinapril (Harris, Tr. 54:2-:15), so the inventors did not face the same issues involved in the Vasotec® process. Standard wet granulation is disclosed in the '450 patent as the preferred manufacturing method (PTX 1, Exs. A and B).

avoid the stabilization problem by minimizing moisture or adding buffering materials to achieve a certain pH, and, in fact, both of these approaches failed to stabilize enalapril. (Brenner, Tr. 633:6-:23).

The extreme difficulty that a person in the field would have faced in 1986 in attempting to carry out the process of stabilizing enalapril with sodium bicarbonate is confirmed by Warner-Lambert's own experience. As discussed above (pp.6-12), even knowing of the existence of Vasotec®, Dr. Murthy's attempt to use sodium bicarbonate to stabilize quinapril failed; the resulting product could not be stabilized against cyclization.

Since Teva has failed to prove, by clear and convincing evidence, that the publicly available Vasotec® information would have enabled one of ordinary skill in the art, as of the time of the '450 invention in August 1986, to carry out a process of stabilizing enalapril with sodium bicarbonate, Teva's invalidity arguments must be rejected. *See, e.g., Hoeksema*, 399 F.2d at 271-72, 275 (expert testimony that processes for preparing the prior art compounds were unavailable to the public, precluded finding anticipation of later patent application claiming those same compounds).

E. Claims 16 And 17 Are Not Obvious

1) Teva has presented no viable obviousness case with respect to claims 16 and 17

Defendant has the burden of proving obviousness by clear and convincing evidence. *Oddzon Prods. Inc.*, 122 F.3d at 1404. To prove obviousness, defendant must submit evidence on each of the three underlying factual inquiries: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; and (3) the differences between the claimed invention and the prior art. *Advanced Display Systems, Inc. v. Kent State University*, 212 F.3d 1272, 1284-85 (Fed. Cir. 2000).

At trial, the only "evidence" offered by Teva on the issue of obviousness was the conclusory testimony by Dr. Schwartz that "a number of other publications" would provide a person of skill with "what you may think is missing." (Schwartz, Tr. 271:2-272:3).

No specific prior art is identified, the scope and content of the art is not discussed and no differences between the claimed invention and prior art are identified. Such conclusory evidence cannot support an obviousness defense. *Upjohn Co. v. Mova Pharm. Corp.*, 225 F.3d 1306, 1311 (Fed. Cir. 2000); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 447-49 (Fed. Cir. 1986).

2) Objective evidence further supports non-obviousness

Even if there were a viable obviousness defense, it would be refuted by Warner-Lambert's showing of so-called "objective evidence" or "secondary considerations." *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). The Federal Circuit has held that such objective evidence may often be the most probative and cogent evidence of non-obviousness in the record and must when present be considered as part of a non-obviousness analysis. *Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556-57 (Fed. Cir. 1985).

One such objective consideration is commercial success. *Id.* In this case, Accupril®, Warner-Lambert's drug product covered by the '450 patent, has enjoyed tremendous success in the marketplace, with annual sales exceeding over half a billion dollars a year. (Harris, Tr. 27:14-:17, 78:9-79:23; Cockburn, Tr. 569:23-570:20). In one month alone, over one-million prescriptions for Accupril® were written. (Cockburn, Tr. 572:1-:5). And Accupril® has captured the number four spot among eleven ACE inhibitors on sale in the United States. (Cockburn, Tr. 570:21-571:12). The fact that this commercially successful product is covered by Warner-Lambert's patent creates a ***presumption*** that commercial success is related to the non-obviousness of the '450 patent. *See J.T. Eaton & Co. v. Atl. Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed. Cir. 1997).

But there is a much more real tie or "nexus" between the commercial success of Accupril® and the '450 patent. As explained by Dr. Harris at trial, quinapril, although a safe and effective ACE inhibitor, experienced such problems with degradation during clinical studies that it was feared at Warner-Lambert that the drug's instability would de-rail the commercial development of the drug. The solution to the stability problem thus eliminated a roadblock in the commercialization of quinapril. (*See* pp. 12-15, above.)

At trial, Teva offered the testimony of an economist, Dr. Cockburn, who testified that he investigated the factors that drove sales of one ACE inhibitor over another once a particular product was already on the market. He concluded that stability was not driving such sales. (Cockburn, Tr. 556:19-:22, 567:10-:17.). Dr. Cockburn's testimony, however, loses sight of the forest for the trees.[16] He admitted that Warner-Lambert could never have commercialized Accupril® in the first place if it had been unable to obtain FDA approval due to stability problems. (Cockburn, Tr. 574:3-:6). Dr. Cockburn also admitted that if a drug formulation determines an end-user value characteristic then it would affect commercial success, and he agreed that an end user in fact values a drug that is able to be marketed.

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[16] Dr. Cockburn admitted he had no background in pharmaceutical formulation, had never reviewed the history of stability problems of ACE inhibitors, and did not even know that stability was a criterion that the FDA looks at before approval of a drug. (Cockburn, Tr. 572:6-573:23.)

(Cockburn, Tr. 574:25-576:20). This of course should be apparent -- physicians would not want to prescribe a drug that is unstable and degrades over time. (Cockburn, Tr. 574:18-:21).

For commercial success to support non-obviousness, the invention need not be the sole cause of the commercial success – it need only be a contributing factor. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1273 (Fed. Cir. 1991). The '450 patented invention was not some "bell or whistle" that the consumer could afford to be indifferent about. Instead, the consumer never would have had the opportunity to purchase Accupril® and enjoy its therapeutic benefits, in the absence of the '450 patented process for stabilizing quinapril, which removed the biggest remaining obstacle to FDA approval and entry in to the marketplace. That is a strikingly clear nexus.

Copying is also evidence of non-obviousness. *Advanced Display Sys.*, 212 F.3d at 1285; *Akamai Techs., Inc. v. Cable & Wireless Internet Servs. Inc.*, 344 F.3d 1186, 1196 (Fed. Cir. 2003). The Court has already held in granting summary judgment of infringement that Teva deliberately copied the '450 patent:

> ***Teva cannot reasonably claim that it did not develop its Quinapril formulations with the '450 patent very much in mind.*** Its personnel knew of the '450 patent since the early 1990's when it was listed in the FDA's 'Orange Book' in connection with the Accupril product. The '450 patent is listed in Teva's patent data base as one of the patents covering the Accupril product. When it

> met in January 1998 to discuss its Quinapril formulation strategy, its Quinapril Team discussed whether in addition to pursuing development of a formulation containing magnesium carbonate and lactose, it should 'develop a totally different formulation in parallel to our current formulation to avoid any potential patent issues with our current strategy.' It elected to pursue the course which ran straight into the '450 patent claims. The Excipient Function Report for Teva's Quinapril formulation describes the function of lactose in Teva's formulation as inhibiting hydrolysis, ***employing the exact words of the '450 patent.***

(PTX 235, pp. 14-15, emphasis added.) Teva's desperate excuse that the FDA encouraged Teva to copy the '450 patent is untenable. Teva has shown absolutely no statute or regulation of the FDA -- because there is none -- that requires or even encourages a generic to copy the formulation of the innovator (as opposed to the active ingredient), and, indeed, most generics attempt as Teva unsuccessfully did to develop a formulation that avoids the innovator's formulation patent.[17]

Lastly, Warner-Lambert also introduced evidence of contemporaneous praise for the patented invention, which is further evidence of non-obviousness. *W.L. Gore*, 721 F.2d at 1555-56. Dr. Harris testified that after the inventors solved the stability problem of quinapril tablets, they received from Warner-Lambert the "meritorious scientific

[17] For example, the Court specifically found in granting summary judgment of infringement that Teva tried, but failed, to develop a stable non-lactose formulation. (*Summary Judgment Opinion*, PTX 235, p.11).

achievement award" which is the "highest award given out in the research division." (Harris, Tr. 76:13-77:16). The fact that a sophisticated drug company chose to single out and recognize a formulation development as exceptional is objective evidence of the non-obviousness of that development.

CONCLUSION

For all of the aforementioned reasons, it is respectfully submitted that Teva did not meet its burden of proving, by clear and convincing evidence, that claims 16 and 17 of the '450 patent are invalid for anticipation or obviousness or that the '450 patent is unenforceable for inequitable conduct, and Warner-Lambert is entitled to judgment accordingly.

Respectfully submitted,

Date: May 28, 2004

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