United States District Court,
D. Delaware.

KEY PHARMACEUTICALS, INC,
Plaintiff.
v.
HERCON LABORATORIES CORPORATION,
Defendant.

Civil Action No. 95-479-RRM

Sept. 30, 1997.

Patentee brought action for infringement of patent for drug-in-adhesive transdermal patch. Following bench trial, the District Court, McKelvie, J., held that: (1) accused patch infringed patent; (2) patent was not anticipated or obvious; and (3) patentee did not engage in inequitable conduct before Patent and Trademark Office (PTO).

Judgment for plaintiff.

4,585,452, 3,742,951, 4,409,206. Original.

Josy W. Ingersoll, James P. Hughes, Jr., Young, Conaway, Stargatt & Taylor, Wilmington, DE; John O. Tramontine, Duane-David Hough, Thomas J. Vetter, John M. Desmarais, and Louis W. Zehil, Fish & Neave, New York City; for plaintiff.

Jack B. Blumenfeld, Morris, Nichols, Arsht & Tunnell, Wilmington, DE; Sheldon I. Landsman, Scott M. Daniels, Brett S. Sylvester, Sughrue, Mion, Zinn, MacPeak & Seas, Washington, D.C.; for defendant.

OPINION

McKELVIE**, District Judge.**

This is a patent case. Plaintiff Key Pharmaceuticals, Inc. ("Key") is the owner of U.S. Patent No. 5,186,938 ("the "8 patent"). Key alleges that defendant Hercon Laboratories Corporation ("Hercon") has infringed claim 14 of the "8 patent. Hercon has denied infringement and has asserted certain affirmative defenses. Hercon has also brought a counterclaim for a declaratory judgment that the "8 patent is invalid, unenforceable, and not infringed. The parties tried this matter to the court from September 30 through October 10, 1996. For the reasons that follow, the court concludes that Hercon has infringed claim 14 and has failed to prove by clear and convincing evidence that the "8 patent is invalid and unenforceable.

I. ***Factual and Procedural Background***

The "8 patent issued on February 16, 1993 following a series of applications, the earliest of which was filed on July 24, 1984. The named inventors are Steven Sablotsky, John Questel, and James Thompson. Claim 14 of the "8 patent, the only claim at issue in this case, is directed to an adhesive transdermal layer comprising a cross-linked acrylic adhesive which is capable of retaining dispersed therein sufficient nitroglycerin to deliver a pharmaceutically effective amount of nitroglycerin to a patient over a 24-hour period. The commercial embodiment of the "8 patent is Key's Nitro-Dur (referred to herein as "Nitro-Dur II"), a drug-in-adhesive transdermal patch that delivers nitroglycerin through the skin of a patient.

A. ***The State of the Art at the Time of the Claimed Invention***

1. ***Reservoir Patches***

Pharmaceutically active drugs can be administered to patients via transdermal patches. These patches are affixed to the skin of a patient, and the drug contained therein passes from the patch's adhesive layer to and through the skin to the patient's circulatory system. The types of drugs that can be administered through such transdermal delivery systems include vasodilators, such as nitroglycerin, which is used to treat angina pectoris. The first commercial transdermal nitroglycerin delivery systems were introduced in the early 1980's. These patches were known as "reservoir" patches because they contained a pouch or matrix wherein the nitroglycerin resided separate from the adhesive layer that adhered the patch to the patient's skin. Due to the pouch or matrix, however, "reservoir" patches tended to be somewhat thick and bulky.

The predecessor of Nitro-Dur II, referred to herein as Nitro-Dur I, was one such reservoir patch. As with other reservoir patches, there were a number of problems associated with Nitro-Dur I. The patch adhered poorly to the skin and had a tendency to leak. It was also uncomfortable to wear. Also, as with other reservoir patches, the process of manufacturing Nitro-Dur I was difficult and time-consuming.

2. ***Drug-In-Adhesive Patches***

At about the time that the first commercial reservoir patches were introduced on the market, others in the field of transdermal drug delivery systems began experimenting with systems in which nitroglycerin was incorporated directly into the adhesive layer, thus eliminating the need for a bulky reservoir. At that time, it was known in the art that drugs could be dispersed within an adhesive layer. Acrylic adhesives were known to be useful for the adhesive layer. Cross-linking of polymers, including acrylic polymers, was almost as old as polymer chemistry itself. According to Key, at least, what was not known in the art was how to combine these elements in such a way so as to incorporate sufficient nitroglycerin into the adhesive layer without dissolving the adhesive.

B. ***The Claimed Invention of*** the "8 Patent

1. ***The Nitro-Dur II Project***

Key began efforts to improve Nitro-Dur I soon after the product was launched with the commencement of a project referred to as the "Nitro-Dur II project." Among those who worked on the Nitro-Dur II project were Steven Sablotsky, one of the "8 patent's named inventors, and Frankie Breslin, a member of Key's clinical staff who worked closely with Sablotsky on the project. The first patch that Key experimented with was a coated two-side adhesive reservoir system in which a drug-permeable membrane was coated with adhesive on both sides. Key believed that coating the membrane on both sides would solve the leakage problems associated with Nitro-Dur I and that, because the external adhesive covered the entire surface of the patch,

the patch could be made smaller than patches that had peripheral adhesives and yet still maintain good adhesion. On April 12, 1983, Sablotsky filed a patent application on the coated two-side system that Key was developing. That patent application eventually issued as U.S. Patent No. 4,585,452 ("the Sablotsky '452 patent") on April 29, 1986.

Nevertheless, the coated two-side system of the Nitro-Dur II project was never introduced to the U.S. market. In fact, the system was never even tested on patients because it failed in laboratory flux studies-tests that measure the amount of drug being released from a patch. Key concluded from the flux studies that the nitroglycerin was not migrating to the external adhesive layer as expected, but instead was migrating to the inner adhesive layer and remaining there.

Key thus abandoned its development of a coated two-side system, and next experimented with a coated one-side system. This system was similar to the coated two-side system except that it did not contain an inner adhesive layer. Instead, the drug-permeable membrane was secured to the plastic backing layer by a heat seal. This system also failed, but this time the failure was due to poor adhesion to the patient. After the failure of the coated two-and one-side systems, Key turned to the development of a drug-in-adhesive nitroglycerin patch, eventually producing the system currently embodied and sold as Nitro-Dur II.

2. ***The Claimed Invention of*** the "8 Patent

As discussed above, at the time of the claimed invention, bilayer transdermal systems comprising a support or backing layer and an adhesive layer containing an active drug were known in the art. According to Key, however, it was not known at the time how to incorporate sufficient nitroglycerin into the adhesive layer without dissolving the adhesive. To determine how to do so, Key hired outside consultants in the field of polymer adhesives. In the course of developing the Nitro-Dur II system, Key employed the expertise of seven consulting firms specializing in adhesives before retaining John Questel and James Thompson, the "8 patent's other two named inventors.

Sablotsky worked with Questel and Thompson in an effort to develop a formulation for the adhesive layer, and sent experimental formulations to Breslin for testing. In a memorandum dated May 8, 1984, Breslin summarized Key's efforts to develop and test the experimental formulations that ultimately led to the creation of the Nitro-Dur II system. Her memorandum describes well over a hundred experimental formulations that failed for, among other things, delivery of sufficient nitroglycerin.

Finally, Key was able to develop an effective formulation and produce the drug-in-adhesive system sold today as Nitro-Dur II. The Nitro-Dur II system comprises an impermeable plastic backing layer laminated to an adhesive layer that contains a pharmaceutically active drug dispersed therein. It is about one-twentieth the thickness of Nitro-Dur I and is smaller and more comfortable for patients to wear. The system does not have a bulky drug-containing reservoir and does not leak like Nitro-Dur I. The manufacturing process of Nitro-Dur II is simple and efficient.

C. ***Key's Prosecution of*** the "8 Patent

On July 24, 1984, Sablotsky, Questel, and Thompson filed an application on the Nitro-Dur II invention with the U.S. Patent and Trademark Office ("PTO"). About a year later, Key filed a number of corresponding foreign applications on the Nitro-Dur II invention.

In early 1986, during the prosecution of the "8 patent, Key received a PCT International Search Report that

listed eight references and rated their degree of materiality to Key's claimed invention. Among the references cited were abstracts of four Japanese Kokais, namely, Japanese Kokai 46959-1983 ("JP '959"); Japanese Kokai 7409-1982 ("JP '409"); Japanese Kokai 7413-1982 ("JP '413"); and Japanese Kokai 7414-1982 ("JP '414"). The PCT report characterized each of the Japanese abstracts as being "of particular relevance such that the claimed invention cannot be considered novel or cannot be considered to involve a novel step." An additional reference cited was German patent DE 3,231,400 ("the DE '400 patent").

In April 1986, Key obtained full English-language translations of the Kokais, and on April 29, 1986, Key was issued the Sablotsky '452 patent. Although Key did not submit the translations or cite the '452 patent to the PTO at that time, Key was then in the process of being acquired by Schering-Plough Corporation. Key's pre-acquisition counsel, Sybil Meloy, testified at her deposition that between March 1, 1986, the date on which the acquisition was announced, and June 1, 1986, the approximate date on which the acquisition was completed, "[t]here was not much work being done ... at Key that was unrelated to the acquisition. It was a totally chaotic condition, the most chaos [that she] had seen in [her] life." Tr. at 1730-31.

Soon after Schering-Plough acquired Key, its patent counsel, John Maitner, assumed the prosecution of the "8 patent. At the time of the acquisition, Maitner was already working on about 20-30 patent prosecutions and their foreign counterparts, in addition to rendering opinions on patent licensing, patentability, and infringement issues. After the acquisition, Maitner became responsible for 10-12 additional pending patent applications and about 50-60 corresponding foreign patent applications.

By the time Maitner had occasion to first review the "8 patent application there were a significant number of prior art references in its file. He did not review each of the references at that time because he "believe[d] the previous attorneys who handled the application had reviewed what they believed was the most relevant art and at that point in time included it in the application." Tr. at 933.

By July 1987, Maimer had become aware of the PCT search report. On June 23, 1988, Maitner filed an amendment in connection with the pending application for the "8 patent. Along with the amendment he submitted a list of the eight prior art references cited in the PCT search report and copies of each of those references, including the English-language abstracts of the four Japanese Kokais and the DE '400 patent. Although by this time Key had obtained a copy of the British counterpart of the DE '400 patent, GB 2 105 990 A ("the GB '990 patent"), Maitner did not cite that patent to the PTO.

Maitner was apparently aware by December 1988 that Key had in its files copies of the full English-language translations of the Kokais. On December 22, 1988, Maitner filed a continuation application with the PTO but did not submit copies of the full English-language translations of the Japanese Kokais even though he was aware that they had not been previously submitted to the PTO. Maimer never provided the PTO with copies of the full English-language translations of the Japanese Kokais even though in some instances he communicated with the PTO just weeks or even days after having reviewed these documents in connection with foreign office actions.

By at least March 1990, Maitner was aware that Key had a copy of the GB '900 patent in its files. In April 1990, Maitner filed another continuation application but did not cite the GB '990 patent to the PTO at that time or any time thereafter.

D. *Key's Action Against Hercon*

Hercon is a generic drug manufacturer seeking approval from the Food and Drug Administration ("FDA") to engage in the commercial manufacture, use, and sale of its generic transdermal nitroglycerin patches, referred to herein as the "NTS-FA patches." On August 7, 1995, Key filed this action, alleging that Hercon has infringed the "8 patent by submitting applications to supplement its conditionally-approved abbreviated new drug applications ("ANDAs") Nos. 88-782, 88-783, and 89-516, which relate to Hercon's generic versions of Nitro-Dur II. Key alleges that these submissions constitute an act of infringement under 35 U.S.C. s. 271(e)(2)(A), which provides, in pertinent part:

It shall be an act of infringement to submit-

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent ...

* * * * * *

if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug ... claimed in a patent ... before the expiration of such patent.

Key seeks a judgment that 1) Hercon's submission of supplements to its ANDAs Nos. 88-782, 88-783, and 89-516 infringes claim 14 of the "8 patent; 2) the "8 patent is valid and enforceable; 3) the effective date of any FDA approval of Hercon's ANDAs Nos. 88-782, 88-783, and 89-516 may not occur before the expiration of the "8 patent; and 4) Hercon is enjoined from making, using, offering for sale, selling, or importing any transdermal nitroglycerin patches that infringe claim 14 of the "8 patent, except as provided for in 35 U.S.C. s. 271(e)(1). The application of s. 35 U.S.C. s. 271(e)(1) would apparently permit Hercon to make, use, offer to sell, or sell patches within the U.S. or import its patches into the U.S. solely for uses reasonably related to the development and submission of other ANDAs that do not relate to Hercon's generic version of Nitro-Dur II.

Hercon has denied infringement and has filed a counterclaim for a declaratory judgment that the "8 patent is invalid, unenforceable and not infringed. From September 30 through October 10, 1996, the parties tried this case before the court. On December 11, 1996, the parties completed post-trial briefing. By letter dated May 12, 1997, the court advised the parties of its proposed construction of claim 14, set forth below, and requested that they file supplemental briefs on the issues of anticipation and obviousness in view of the court's interpretation. The parties completed supplemental briefing on June 27, 1997.

II. ***Discussion***

A. ***Claim Construction***

[1] [2] [3] Claim construction is a matter for the court. Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed.Cir.1995) (en banc), *aff'd,* 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). Claims are construed from the vantage point of a person of ordinary skill in the art at the time of the invention. Id., at 986. A term of a patent claim is interpreted as having the meaning that it would be given by one of ordinary skill in the art unless it is apparent from the patent and the prosecution history that the inventor intended a different meaning. Hoechst Celanese Corp. v. BP Chems. Ltd., 78 F.3d 1575, 1578 (Fed.Cir.), *cert. denied,* 519 U.S. 911, 117 S.Ct. 275, 136 L.Ed.2d 198 (1996).

[4] [5] In construing a claim, a court looks first to the intrinsic evidence of record, namely, the language of

the claims of the patent, both asserted and nonasserted, the specification, and the prosecution history. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996). In most cases, an analysis of the intrinsic evidence alone will resolve any dispute concerning the meaning of a term. Id. at 1583. However, extrinsic evidence such as expert testimony may be considered if needed to assist the court in understanding the technology at issue or in determining the meaning or scope of technical terms in a claim. Hoechst Celanese, 78 F.3d at 1579. A court may require expert testimony in order to understand how a person of ordinary skill in the pertinent art would construe a claim. *See* id. at 1578-79.

Claim 14 is the only claim of the "8 patent at issue in this case. Claim 14 depends from claim 13, which in turn depends from claim 12, which reads as follows:

An adhesive transdermal layer for the sustained release of a pharmaceutically active drug to the skin of a human patient, comprising:

a pharmaceutically active drug-containing essentially planar sheet of an at least partially cross-linked acrylic adhesive, said essentially planar sheet comprising a flexible self-supporting cross-linked acrylate polymer of sufficient adhesivity, durability and strength whereby intimate diffusional contact with skin of the patient is maintained for a period of at least about 24 hours without destruction of the physical integrity thereof, said essentially planar sheet being capable of retaining dispersed therein sufficient pharmaceutically active drug to deliver to the skin a pharmaceutically effective amount of said pharmaceutically active drug over a 24-hour time interval, without dissolution of the at least partially cross-linked acrylic pressure-sensitive adhesive.

Claim 13 limits claim 12 by requiring that the "pharmaceutically active drug" be a vasodilator. Claim 14 limits claim 13 by requiring that said vasodilator be nitroglycerin. Thus, claim 14 is essentially claim 12 with the term "nitroglycerin" substituted for "pharmaceutically active drug."

The meaning of two phrases of claim 14 are in dispute. The parties dispute the meaning of "whereby intimate diffusional contact with skin of the patient is maintained for a period of at least about 24 hours without destruction of the physical integrity thereof" in connection with the issue of infringement. The parties dispute the meaning of "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" in connection with the issue of validity.

1. ***The Meaning of "Whereby Intimate Diffusional Contact With Skin of the Patient is Maintained for a Period of About at Least 24 hours Without Destruction of the Physical Integrity Thereof"***

[6] Hercon contends that the phrase "whereby intimate diffusional contact with skin of the patient is maintained for a period of at least about 24 hours without destruction of the physical integrity thereof" means that the adhesive transdermal layer described in claim 14 *must* maintain contact with the skin of a patient for at least about 24 hours. Hercon argues that, if claim 14 requires that the adhesive transdermal layer merely be *capable of* maintaining contact with the skin of a patient for at least about 24 hours, the inventors would have used language such as "capable of" as they did in other parts of the specification and in claim 14 itself. *See e.g.,* col. 3, lines 39-41; col. 5, lines 38-40; col. 12, lines 16-18.

Hercon's interpretation is not supported by the plain language of claim 14. When placed in context, the disputed language reads "said essentially planar sheet comprising a flexible self-supporting cross-linked acrylate polymer of sufficient adhesivity, durability and strength whereby intimate diffusional contact with

skin of the patient is maintained for a period of at least about 24 hours without destruction of the physical integrity thereof." This portion of claim 14 thus concerns the *sufficiency* of the adhesive layer. It is not a directive that the layer maintain contact with the skin of a patient for at least about 24 hours. Any ambiguity, however, is resolved by resort to the specification. *See* Vitronics, 90 F.3d at 1582. ("The specification acts as a dictionary when it expressly defines terms used in the claims of when it defines terms by implication."). The specification states that one of the objects of the invention is:

to provide an adhesive transdermal dosage system ... containing ... [an] essentially planar sheet comprising a flexible self-supporting cross-linked acrylate polymer of sufficient adhesivity, durability, and strength where the skin of the patient *can be maintained* in intimate diffusional contact therewith, the layer capable of retaining a quantity of pharmaceutically active drug over a period of 24 hours without destruction of the physical integrity of the sheet....

See col. 4, lines 35-48 (emphasis added). This statement is nearly identical to the disputed language and thus serves to clarify its meaning. Accordingly, the court concludes that claim 14 does not require that the adhesive transdermal layer maintain contact with the skin of a patient for at least about 24 hours, but rather only that the layer be capable of maintaining contact with the skin of a patient for that amount of time.

2. *The Meaning of "Sufficient [*Nitroglycerin*] to Deliver to the Skin a Pharmaceutically Effective Amount of [*Nitroglycerin*] Over a 24-Hour Time Interval*"

Hercon contends that the phrase "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" means an amount of nitroglycerin sufficient to provide a patient with 2.5 to 15 mg of nitroglycerin per day. Hercon's interpretation is based on the testimony of its expert witness, Dr. Richard H. Guy. Dr. Guy is a Ph.D. in pharmaceutical chemistry. He was an assistant professor of pharmacy and pharmaceutical chemistry at the University of California, San Francisco from 1980 until 1987, when he was granted tenure and promoted to associate professor there. In July of this year, he took a new post as the scientific director of an interuniversity research center outside of Geneva, in France. The focus of the work going on in this institute is the design and development of drug delivery systems. Dr. Guy is specifically responsible for a group within the institute that will be working on the delivery of drugs through the skin. Tr. at 1004-10.

At trial, Dr. Guy testified as to his understanding of the meaning of the phrase "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" to one of ordinary skill in the art of transdermal delivery systems at the time of the claimed invention. He explained that, as a general matter, there is a correlation between the concentration of a drug in a patient's blood and the effect that the drug produces. Therefore, it is desirable to sustain a certain concentration of drug in the blood over a specific period of time. That concentration of drug ideally falls in what is referred to as "the therapeutic window." The therapeutic window is a concentration of drug above that which is minimally effective and below that which is minimally toxic. The goal of administering a drug is therefore to achieve and sustain over a desired period of time a concentration that falls within the therapeutic window. Tr. at 1093-96.

Dr. Guy concluded that the term "pharmaceutically effective amount" means an amount which allows sustained drug delivery and which provides a concentration of drug that falls within the therapeutic window, and that the phrase "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" means the amount of nitroglycerin required to sustain the

desired concentration over a 24-hour period. Dr. Guy further testified that there is nothing in the "8 patent or its file history that would lead him to a different conclusion because, in his opinion, the patent does not expressly disclose any numerical values that give meaning to the phrase. Tr. at 1096-97.

Dr. Guy testified that, in determining a numerical value for the term "pharmaceutically effective amount," one of ordinary skill in the art at the time of the claimed invention would have looked to the transdermal delivery systems conditionally approved by the FDA for guidance. He explained that such systems delivered between 2.5 and 15 mg of nitroglycerin per day. Tr. at 1098-99. Hercon thus concludes that one of ordinary skill in the art at the time of the claimed invention would have interpreted "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" to include, at least, an amount sufficient to provide a patient with 2.5 to 15 mg of nitroglycerin per day; that is, 2.5 to 15 mg of nitroglycerin, plus an excess amount to ensure that the desired amount is delivered.

Key, on the other hand, contends that the "8 patent discloses express numerical values for what is meant by "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval." First, Key contends that the phrase means nitroglycerin delivered at a flux rate of 0.3 to about 0.7 mg per square centimeter per day. Key's contention is based on a statement in the specification of the "8 patent that an "object of the invention is to provide a dosage system wherein nitroglycerin is delivered to the skin in an amount of from 0.3 to about 0.7 mg per square centimeter of the first component layer per 24-hour time interval." *See* col. 4, lines 67-68; col. 5, lines 1-3.

[7] [8] In construing a disputed term in a claim, a court looks first to the patent's claims, both asserted and nonasserted. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996). The invention of the "8 patent is an adhesive transdermal delivery system containing two component layers. Independent claim 1 is directed to a bilayer system containing both an adhesive layer and a backing layer. Independent claim 12 is directed to only an adhesive transdermal layer. With respect to the adhesive layer, the language of claim 1 is virtually identical to the language of claim 12, except that the term "nitroglycerin" is substituted for "pharmaceutically active drug." Claim 3, which depends from claim 1, requires that the nitroglycerin be "delivered to the skin in an amount of from about 0.3 to 0.7 mg per square centimeter ... per 24-hour time interval." Under the doctrine of claim differentiation, "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" as that term appears in claim 1 must be presumed to have a different meaning from the flux rate stated in claim 3. *See e.g.,* Tandon Corp. v. United States Internat'l Trade Comm'n, 831 F.2d 1017, 1023 (Fed.Cir.1987) ("There is presumed to be a difference in meaning and scope when different words or phrases are used in separate claims."). Indeed, if claim 1 were read to require nitroglycerin delivered in an amount of 0.3 to about 0.7 mg per square centimeter per day, then claim 3 would be superfluous. *See id.* ("To the extent that the absence of such difference in meaning and scope would make a claim superfluous, the doctrine of claim differentiation states the presumption that the difference between claims is significant."). Because the claims of a patent must be interpreted in a consistent manner, Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1579 (Fed.Cir.1995), it must be presumedthat the phrase "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" in claim 12 likewise does not mean nitroglycerin delivered in an amount of 0.3 to about 0.7 mg per square centimeter per day.

Key argues that the presumption created by the doctrine of claim differentiation is overcome by a statement in the specification that one of the objects of the invention is to deliver nitroglycerin in an amount of 0.3 to about 0.7 mg per square centimeter per day. However, the mere fact that the specification states that this flux rate is an object of the invention does not require that claim 14 be read to include that flux rate. See Intel

Corp. v. United States Internat'l Trade Comm'n, 946 F.2d 821, 836 (Fed.Cir.1991) (refusing to read numerical value described as a goal of the invention into claims where limitation not contained in claims). Although Key relies heavily on United States v. Adams, 383 U.S. 39, 86 S.Ct. 708, 15 L.Ed.2d 572 (1966), where the Supreme Court considered a stated object of the invention at issue in construing a claim, the Court did not simply read the stated object into the claims at issue, as Key proposes the court do here, but rather considered the stated object together with certain inferences that could be drawn from the language of the patent's claims. *See* 383 U.S. at 48-49, 86 S.Ct. at 712-13. Here, Key has not identified any other support for reading the flux rate stated as an object of the invention into claim 14. Accordingly, the court concludes that Key has failed to overcome the presumption and that claim 14 does not require that nitroglycerin be delivered in an amount of 0.3 to about 0.7 mg per square centimeter per day.

Key also contends that the phrase "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" means nitroglycerin incorporated into the cross-linked adhesive in an amount of about 20 to 50 or 60% by weight based on the weight of the first component layer. Key bases its contention upon the statement in the specification that "[t]he most preferred embodiment is nitroglycerin incorporated in the cross-linked adhesive and especially incorporated in an amount of about 20 to 50 or 60% by weight based on the weight of the first component layer." *See* col. 7, lines 11-15.

[9] Key overlooks the well-established principle that claims are not necessarily limited to the preferred embodiment or specific examples disclosed in the specification. *See* Ekchian v. Home Depot, Inc., 104 F.3d 1299, 1303 (Fed.Cir.1997). Key has not identified anything else in the specification or prosecution history that suggests that "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" means nitroglycerin incorporated into the cross-linked adhesive in an amount of about 20 to 50 or 60% by weight based on the weight of the first component layer. Accordingly, the court concludes that claim 14 does not require that nitroglycerin be incorporated into the cross-linked adhesive in an amount of about 20 to 50 or 60% by weight based on the weight of the first component layer.

[10] Finally, Key contends that claim 14 requires that the adhesive layer described therein be capable of delivering a pharmaceutically effective amount of nitroglycerin in a system having a 5 cm^2 surface area. Key's contention is based on a statement in the specification of the "8 patent that "[t]he present invention allows for the delivery of enough pharmaceutically active drug such as nitroglycerin to provide efficacy with a dosage system having a 5 cm^2 surface area...." *See* col. 9, lines 51-54. Key's interpretation, however, would require importing an extraneous limitation from the specification into claim 14, which is wholly improper. *See* E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co., 849 F.2d 1430, 1433 (Fed.Cir.1988). An extraneous limitation is one "read into a claim from the specification wholly apart from any need to interpret what the patentee meant by particular words or phrases in the claim." *Id*. Nothing in claim 14 or the specification suggests that the surface area of the adhesive layer should be considered in interpreting the phrase "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval."

Having rejected Key's proposed claim construction, the court must determine whether to adopt Hercon's proposed claim construction. At trial, Key offered the opinions of their expert, Dr. John K. Beasley, to counter Hercon's proposed construction. Dr. Beasley received a Ph.D. in physical chemistry from Massachusetts Institute of Technology in 1951. He worked for 35 years for E.I. DuPont de Nemours as a research chemist. His work there focused on research and development of various polymers. Since 1986, Dr.

Beasley has worked as a technical consultant and expert witness on several patent matters.

[11] Dr. Beasley opined that one of ordinary skill in the art at the time of the claimed invention would have interpreted the phrase "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" to require the numerical values that the court has concluded should not be read into claim 14. *See* Tr. at 1454-1507. Because Dr. Beasley did not otherwise undermine the testimony of Dr. Guy, the court concludes that the phrase "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" means an amount sufficient to provide a patient with 2.5 to 15 mg of nitroglycerin per day-that is, 2.5 to 15 mg of nitroglycerin, plus an excess amount to ensure that the desired amount is delivered.

B. ***Infringement***

[12] Hercon argues that its NTS-FA patches do not infringe claim 14 of the "8 patent because, whereas claim 14 requires that the adhesive layer of the claimed invention maintain contact with the skin of a patient for a 24-hour period, Hercon's NTS-FA patches are to be worn for only 12 to 14 hours. As discussed above, however, the court has concluded that claim 14 does not require that the adhesive layer maintain contact with the skin of a patient for at least about 24 hours, but rather only that the layer be capable of maintaining contact with the skin of a patient for that amount of time.

At trial, Dr. Beasley testified that Hercon's NTS-FA patches can be worn for 24 hours without destruction of the adhesive layer. Tr. at 474-75; 487. His testimony was based on his review of clinical studies conducted by Hercon as well as a personal study he conducted by wearing an NTS-FA patch for three days. Hercon offered no evidence to the contrary. In fact, Dr. Guy testified that it was his understanding that Hercon's patches can be worn for 24 hours without destruction of the adhesive layer. Tr. at 1219. Accordingly, the court finds that Key has proved by a preponderance of the evidence that Hercon's NTS-FA patches infringe claim 14 of the "8 patent.

C. ***Validity***

[13] Hercon contends that the "8 patent is invalid on three grounds: 1) anticipation; 2) obviousness; and 3) failure to disclose the best mode. A party asserting the defense of invalidity bears the burden of proving such defense by clear and convincing evidence. Northern Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 935 (Fed.Cir.1990) Clear and convincing evidence is that which proves in the mind of the trier of fact "an abiding conviction that the truth of [the] factual contentions is highly probable." Intel Corp. v. United States Internat'l Trade Comm'n, 946 F.2d 821, 830 (Fed.Cir.1991).

1. ***Anticipation and Obviousness***

Hercon asserts that claim 14 is anticipated by six prior art references, none of which were disclosed in full to the PTO during the prosecution of the "8 patent: 1) JP '959; 2) JP '409; 3) JP '413; 4) JP '414; 5) the Sablotsky '452 patent, and 6) the GB '990 patent. Hercon also asserts that claim 14 is further made obvious by two other references, U.S. Patent No. 3,742,951 ("the Zaffaroni '951 patent") and U.S. Patent No. 4,409,206 ("the Stricker '206 patent"), when considered in light of numerous prior art references that disclose the desirability and practice of cross-linking drug-containing acrylic adhesives.

[14] [15] [16] A patent claim is anticipated if each element of the claimed invention is disclosedin a single reference in the arrangement recited in the asserted claim. Richardson v. Suzuki Motor Co., 868 F.2d 1226,

1236 (Fed.Cir.1989). A party asserting that a patent claim is anticipated must demonstrate, among other things, identity of invention. Minnesota Mining & Manuf. v. Johnson & Johnson Orthopaedics, Inc., 976 F.2d 1559, 1565 (Fed.Cir.1992). One who seeks to establish identity of invention must show that each element of the claim at issue is found, either expressly or under principles of inherency, in a single prior art reference, or that the claimed invention was previously known or embodied in a single prior art device or practice. *Id*. There must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the field of the invention. Scripps Clinic & Research Foundation v. Genentech, Inc., 927 F.2d 1565, 1576 (Fed.Cir.1991). The prior art reference must also be enabling, thereby placing the allegedly disclosed matter in the possession of the public. Akzo N.V. v. United States Internat'l Trade Comm'n, 808 F.2d 1471, 1479 (Fed.Cir.1986).

[17] [18] A patent claim is invalid as obvious if the differences between the claimed invention as a whole and the prior art are such that the subject matter as a whole would have been obvious at the time of the invention to a person having ordinary skill in the art. 35 U.S.C. s. 103. In determining whether an invention was obvious, the following factors are considered: 1) the scope and content of the prior art; 2) the level of ordinary skill in the art; 3) the differences between the claimed subject matter and the prior art; 4) any objective evidence of nonobviousness. Ashland Oil, Inc. v. Delta Resins & Refractories, 776 F.2d 281, 291 (Fed.Cir.1985). "Obvious to try" must not be equated with obviousness. Gillette Co. v. S.C. Johnson & Son, Inc., 919 F.2d 720, 725 (Fed.Cir.1990).

[19] For the reasons set out below, the court concludes that Hercon has failed to prove by clear and convincing evidence that any of the references on which it relies anticipate or render obvious claim 14. The court notes, however, that it has not examined the record to determine the extent of any objective indicia of nonobviousness. The court has not done so because, even in the absence of any indicia of nonobviousness, the court would nevertheless conclude that Hercon has failed to prove that claim 14 is obvious because Hercon has fallen far short of demonstrating that the prior art would have suggested to one of ordinary skill in the art of transdermal delivery systems how to make the invention of the "8 patent.

a. *JP '959*

JP '959 discloses a transdermal acrylic adhesive layer for administering a drug across the skin that is at least partially cross-linked and is flexible and self-supporting. It discloses the use of nitroglycerin and states that the amount of drug should be suitably selected to obtain the therapeutic or other effect for which it is administered. At trial, Dr. Guy testified that one skilled in the art would have interpreted such a disclosure to mean "a pharmaceutically effective amount," as recited in the "8 patent. Tr. at 1168-69. Example 3 of JP '959 discloses a 100 cm^2 patch with a cross-linked acrylic adhesive layer containing 40 mg of nitroglycerin.

Hercon contends that both the main text of JP '959 and Example 3 anticipate claim 14. At trial, Dr. Guy testified that the main text of JP '959 discloses an adhesive layer capable of holding sufficient nitroglycerin to deliver to the skin a pharmaceutically effective amount of nitroglycerin over a 24-hour time interval because it directs one skilled in the art to adjust the amount of nitroglycerin in the layer to achieve a "therapeutic effect." *See* Tr. at 1173. To anticipate, however, a prior art reference must be enabling. The mere fact that JP '959 directs one to adjust the amount of nitroglycerin as necessary does not mean that the reference necessarily enables one to incorporate sufficient nitroglycerin to deliver at least 2.5 mg of nitroglycerin per day into the adhesive layer. As Dr. Beasley testified, it is impossible to predict with certainty how different chemicals will mix in a polymer system. Tr. at 1451-52. For instance, the addition of too much nitroglycerin can cause an adhesive layer to dissolve. Tr. at 1451-52. Thus, one cannot simply

assume that nitroglycerin can be incorporated into an adhesive layer without adversely affecting the other properties of the adhesive layer. Hercon never attempted to demonstrate otherwise, and thus has failed to show that the main text of JP '959 anticipates claim 14.

Hercon has also failed to prove by clear and convincing evidence that Example 3 anticipates claim 14. At trial, Dr. Guy attempted to demonstrate on direct examination that the 100 cm^2 patch disclosed in Example 3 could deliver at least 0.1 mg of nitroglycerin per hour, the minimum amount currently approved by the FDA, and the amount delivered by the Nitro-Dur II system, by performing certain calculations to show that the Nitro-Dur II system and the disclosed patch delivered nitroglycerin at the same rate. On cross-examination, Dr. Guy conceded that he had made certain errors in his calculations. Tr. at 1237-1313. During his testimony, Dr. Beasley purported to correct Dr. Guy's errors, and calculated that the 100 cm^2 patch disclosed in Example 3 would deliver at most only 1.92 mg of nitroglycerin per day. Tr. at 1574-1633. He went on to calculate that such a patch would need to be 125 cm^2 in order to deliver 2.5 mg of nitroglycerin per day. Tr. at 1586.

Relying on Dr. Beasley's testimony, Hercon now contends in its supplemental briefs that Example 3 teaches the delivery of "a pharmaceutically effective amount" of nitroglycerin as recited in claim 14. Hercon reasons as follows. Dr. Beasley calculated that the Example 3 patch would deliver 1.92 mg of nitroglycerin per day by using a parameter based on a delivery rate of 0.1 mg of nitroglycerin per hour, or 2.4 mg of nitroglycerin per day. If one were to perform Dr. Beasley's calculations using a parameter based on a delivery rate of 2.5 mg per day, one would calculate that the Example 3 patch would deliver 2.0 mg of nitroglycerin per day. A delivery rate of 2.0 mg per day satisfies the bioequivalence requirements of the FDA for patient efficacy for an ANDA applicant. An ANDA patch is considered by the FDA to be bioequivalent to an approved patch if it delivers the same amount of drug, plus or minus 20 percent. Thus, a patch could vary by as much as 20 percent and still be considered bioequivalent to an approved patch-that is, it would still be considered pharmaceutically effective and thus would be labeled by the FDA as 2.5 mg per day. 2.5 mg per day less 20 percent is 2.0 mg per day.

The issue of bioequivalency, however, is actually a matter of claim construction. That is, Example 3 might be said to disclose the delivery of "a pharmaceutically effective amount" of nitroglycerin as recited in claim 14 if that term were construed to cover amounts that the FDA would consider bioequivalent to 2.5 to 15 mg per day. At trial, however, Hercon did not offer any evidence that one of ordinary skill in the art would have so construed "a pharmaceutically effective amount." Rather, Dr. Guy testified only that one of ordinary skill would have construed "sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour time interval" as an amount sufficient to deliver between 2.5 and 15 mg of nitroglycerin per day. Thus, there is no support in the record for construing "a pharmaceutically effective amount" of nitroglycerin as at least 2.0 mg of nitroglycerin per day.

In any event, Hercon has failed to establish that the patch disclosed in Example 3 is even capable of delivering 2.0 mg of nitroglycerin per day. In comparing the Nitro-Dur II system and the Example 3 patch to show that the Example 3 patch would deliver at least 2.4 mg of nitroglycerin per day, Dr. Guy admitted that he was *assuming* that one of the values used in his calculations, the proportionality constant, would be the same for both systems. His assumption was based on his conclusion that the adhesive layers of both systems were similar. Tr. at 1272-73. In correcting Dr. Guy's calculations and arriving at the 1.92 figure, Dr. Beasley used the proportionality constant provided by Dr. Guy. Tr. at 1579. He testified, however, that the proportionality constant would be different if the chemical composition of the adhesive layers being

compared were not similar. Tr. at 1578-79; 1598. Dr. Guy never explained why the layers of Nitro-Dur II and the Example 3 patch could be considered similar so as to permit him to assume that the proportionality constant would be the same. Nitro-Dur II contains 37.4% nitroglycerin and 56.8% acrylic polymers, the 5.8% balance made up of thickener, cross-linker, and water. By contrast, the Example 3 patch contains only 2% nitroglycerin and approximately 25% acrylic polymers, and also contains, in addition to a cross-linker, significant amounts of polyethylene glycol (about 60%) and polyoxypropylated sorbitol (about 10%), two chemicals not present in Nitro-Dur II Accordingly, the court concludes that Dr. Guy's calculations, based as they are on an unverified assumption concerning the proportionality constant, do not serve as clear and convincing evidence that the Example 3 patch is actually capable of delivering at least 2.0 mg of nitroglycerin per day.

Hercon argues that even if the Example 3 patch does not disclose the incorporation of sufficient nitroglycerin to deliver at least 2.5 mg of nitroglycerin per day, it would have been obvious to one skilled in the transdermal art to incorporate such an amount in the disclosed system by either increasing the surface area of the patch or by increasing the concentration of nitroglycerin in the adhesive layer of the patch.

As discussed above, however, one cannot simply conclude that nitroglycerin can be incorporated into an adhesive layer without adversely affecting the other properties of the adhesive layer. Hercon never attempted to demonstrate that the adhesive layer disclosed in Example 3 could incorporate a higher concentration of nitroglycerin without dissolving. Thus, Hercon has not shown that it would have been obvious to incorporate sufficient nitroglycerin to deliver at least 2.5 mg of nitroglycerin per day in the Example 3 patch merely be increasing the concentration of nitroglycerin in the patch.

Neither has Hercon shown that it would have been obvious to incorporate sufficient nitroglycerin by increasing the surface area of the patch. Hercon contends that Dr. Beasley's calculations demonstrate that a patch constructed according to Example 3 with an area of 125 cm^2 would deliver 2.0 mg of nitroglycerin per day, and argues that a minor increase in the size of the patch would result in the delivery of 2.5 mg of nitroglycerin per day. As discussed above, Hercon has not provided clear and convincing evidence that such a patch would be capable of delivering 2.0 mg of nitroglycerin per day. Even if Hercon were to contend that a greater increase in the surface area of the patch would result in the delivery of 2.5 mg of nitroglycerin per day, Hercon has not demonstrated that such a patch would otherwise meet claim 14's recitation that the adhesive layer be capable of maintaining intimate diffusional contact with the skin of a patient for 24 hours. At trial, Key introduced an excerpt of a report by Dr. Gordon Flynn, a pharmaceutical expert for Key, in which he stated that patches over a certain size would not meet that requirement because they would not stay in place as a result of stretching occurring through body movement. Tr. at 1359. Because Hercon has failed to establish with certainty how much the patch disclosed in Example 3 would have to be increased in order to deliver at least 2.5 mg of nitroglycerin per day, the court is unable to conclude whether such a patch would otherwise meet claim 14's limitations.

b. *JP '409, JP '413. and JP '414*

JP '409, JP '413, and JP '414 each disclose bilayer transdermal devices for administering a drug across the skin. JP '409 and JP '413 each disclose a cross-linked acrylic adhesive layer. JP '414 discloses an adhesive layer that may be cross-linked. Each reference discloses an adhesive layer containing a drug which may be a vasodilator such as nitroglycerin. Although the references do not provide any numerical values for the amount of nitroglycerin to be incorporated, they do disclose that the amount of drug should be chosen to provide a patient with "the therapeutic or other effect" for which the drug is administered.

Key argues that Hercon has failed to prove by clear and convincing evidence that either JP '409, JP '413, and JP '414 disclose a system capable of delivering at least 2.5 mg of nitroglycerin per day. The court agrees. At trial, Dr. Guy testified that these references disclose an adhesive layer capable of holding sufficient nitroglycerin because they direct one skilled in the art to adjust the amount of nitroglycerin in the layer to achieve a "therapeutic effect." See Tr. at 1148-49; 1173. As discussed above, however, the mere fact that these references direct one to adjust the amount of nitroglycerin to achieve such an effect does not mean that they necessarily enable one to incorporate into the adhesive layer sufficient nitroglycerin to deliver at least 2.5 mg of nitroglycerin per day. As Dr. Beasley testified, it is impossible to predict with certainty how different chemicals will mix in a polymer system. Tr. at 1451-52. Thus, one cannot simply assume that nitroglycerin can be incorporated into an adhesive layer without adversely affecting the other properties of the adhesive layer. Again, Hercon never attempted to demonstrate otherwise, and thus failed to satisfy its burden of proof.

Hercon argues that JP '409, JP '413, and JP '414 each render claim 14 invalid because it would have been obvious to one skilled in the art to either increase the size of the patches disclosed in the examples of these references or to adjust the concentration of the drug disclosed in those patches in order to deliver at least 2.5 mg of nitroglycerin per day. Again, one cannot assume that the concentration of nitroglycerin in an adhesive layer can be increased without a deleterious effect on the integrity of that layer. In addition, Hercon never attempted to show how much nitroglycerin the disclosed patches were capable of delivering. Hercon is therefore unable to establish with certitude how much the patches would need to be increased in order to deliver at least 2.5 mg of nitroglycerin per day. As discussed above, patches over a certain size might not otherwise meet claim 14's recitation that the adhesive layer be capable of maintaining intimate diffusional contact with the skin of a patient for 24 hours. Because Hercon has failed to establish with certainty how much the patches would have to be increased in order to deliver at least 2.5 mg of nitroglycerin per day, the court is unable to conclude whether such patches would meet that limitation. Hercon has thus failed to show by clear and convincing evidence that either JP '409, JP '413, or JP '414 render claim 14 obvious.

c. *Sablotsky* '452 Patent

The Sablotsky '452 patent discloses a transdermal delivery system that comprises a laminate structure having a plurality of layers which are: 1) a first adhesive layer having dispersed therein a high concentration of drug; 2) a semipermeable barrier layer; 3) a second adhesive layer; 4) an aqueous drug reservoir solvent system that contains the drug to be administered; and 5) a backing layer.

The patent discloses cross-linked acrylic adhesive layers and nitroglycerin as a preferred drug. It further discloses that the drug is to be incorporated into the adhesive layer to provide a systemic dosage over 24 hours. Although the patent discloses a reservoir system, as opposed to a drug-in-adhesive system such as that disclosed by the "8 patent, Hercon nevertheless contends that the '452 patent discloses an adhesive layer "capable of retaining dispersed therein sufficient [nitroglycerin] to deliver to the skin a pharmaceutically effective amount of [nitroglycerin] over a 24-hour interval," as required by claim 14. Hercon argues that, because the nitroglycerin that diffuses from the '452 system into the skin of a patient must pass through the first adhesive layer which delivers the nitroglycerin over a 24-hour period, the first adhesive layer is capable of retaining dispersed therein sufficient nitroglycerin as required by claim 14.

Hercon, however, has failed to show that the '452 patent is enabling. At trial, Key adduced evidence that the transdermal delivery system disclosed in the Sablotsky '452 patent was considered by Key to be a complete

failure. Frankie Breslin, who was integrally involved in the development of the coated two-side system, which Key contends is the subject of the '452 patent, testified that every single patch made according to the '452 patent failed for lack of adequate drug delivery. Tr. at 180-84. Key also introduced deposition testimony from Dr. Allyn Golub, the head of Key's clinical department, who stated that the coated two-side systems that were tested "weren't successful and that's because they were unstable. The drug migrated in [a] way that was unacceptable." Tr. at 300.

In post-trial briefing, Hercon argues that Key adduced no evidence that the coated two-side systems referred to by Breslin and Dr. Golub are the subject of the '452 patent. Hercon, however, bore the burden of proving that the '452 patent was enabling, but produced no evidence in that regard. Accordingly, the court concludes that Hercon has failed to prove by clear and convincing evidence that the Sablotsky '452 patent anticipates claim 14.

In its supplemental post-trial brief, Hercon contends that the Sablotsky '452 patent renders claim 14 invalid because, in the absence of unexpected results, it would have been obvious to one skilled in the art to "vary the thickness and distributions to provide the adhesive layer with an amount of drug that delivers 2.5 mg of nitroglycerin per day." Hercon, however, fails to cite to any evidence of record in support of its contention. Moreover, as discussed above, Hercon has failed to prove that the Sablotsky '452 patent is enabling. For these reasons, the court concludes that Hercon has failed to prove by clear and convincing evidence that the Sablotsky '452 patent renders claim 14 obvious.

d. *GB '990 Patent*

The GB '990 patent discloses a transdermal adhesive layer that may comprise a cross-linked acrylic adhesive and nitroglycerin in an amount ranging from 0.1-20% and preferably 0.5-15%. Hercon contends that the GB '990 patent thus discloses an amount of drug in excess of the amount needed to deliver 2.5 mg of the drug per day.

Key points out, however, that the examples in the GB '990 reference contain only 2.7-5.3% nitroglycerin, and contends that the reference does not teach how to incorporate up to 20% nitroglycerin without dissolution of the adhesive layer. Hercon never attempted to demonstrate that the adhesive layer disclosed by the GB '990 patent could actually incorporate enough nitroglycerin to deliver at least 2.5 mg per day without dissolving, and thus has failed to meet its burden of establishing anticipation by clear and convincing evidence.

Hercon also contends that the GB '990 patent renders claim 14 invalid because it would have been obvious to one skilled in the art to either increase the size of the patch or to adjust the concentration of drug of the patch disclosed therein in order to deliver at least 2.5 mg of nitroglycerin per day. The court rejects Hercon's contention for the same reason it concludes that neither JP '409, JP '413, or JP '414 render claim 14 obvious.

e. *Zaffaroni* '951 Patent

The Zaffaroni '951 patent, which was before the PTO during Key's prosecution of the "8 patent application, discloses a medical bandage comprising a backing layer and a pressure sensitive acrylic layer. The patent discloses four types of transdermal patches. One of these examples has microcapsules of a drug dispersed throughout the adhesive layer. The remaining three are more traditional reservoir-type patches. The patent also discloses that the daily amount of nitroglycerin to be delivered to treat patients for angina should be between 0.1 to 5 mg per day. However, the patent does not disclose a cross-linked acrylic adhesive layer.

Hercon contends that the '951 patent discloses each recitation of claim 14, except for the pressure-sensitive adhesive being cross linked. Hercon goes on to argue that it would have been obvious to cross-link the acrylic adhesive in view of any of numerous prior art references which disclose and suggest that it is conventional, well-known, and desirable to cross-link a drug-containing pressure-sensitive acrylic adhesive that is to be applied to the skin.

However, the '951 patent differs from the "8 patent in another significant way. It is a reservoir patch, as opposed to a simple bilayer patch. Even in the example within the '951 patent which discloses microcapsules within the adhesive layer, these are simply a number of very small reservoirs. This system does not make obvious the "8 drug-in-adhesive system. Cross-linking the adhesive of the '951 patent would not result in the system invented in the "8 patent.

Even if Hercon were right about the obviousness of cross-linking the adhesive in the '951 patent, Hercon has not identified a single prior art reference that it has shown teaches a cross-linked acrylic layer capable of delivering at least 2.5 mg of nitroglycerin per day. Thus, Hercon has not shown that such a system would necessarily be capable of delivering nitroglycerin in that amount. Accordingly, Hercon has not shown that claim 14 is rendered obvious by the '951 patent.

f. ***Stricker*** '206 Patent

The Stricker '206 patent, which was also before the PTO during Key's prosecution of the "8 patent application, discloses a transdermal delivery system comprising a skin-compatible polyacrylate film that swells in water and that contains a pharmaceutical agent, such as nitroglycerin. While the patent does not specifically disclose a delivery of 2.5 mg/day, it does deliver 0.08 mg/cm^2/day, and it discloses that the size of the patch can be from 4 to 60 cm^2. Thus a patch of 32 cm^2 per day would deliver the required daily dosage. The patent, however, does not disclose a cross-linked acrylic adhesive.

Hercon contends that it would have been obvious to cross-link the acrylic adhesive for the same reasons it gave in connection with the Zaffaroni '951 patent. For the reasons discussed above in connection with that reference, the court concludes that Hercon has failed to prove by clear and convincing evidence that the '206 patent renders claim 14 obvious.

g. ***Combination of Prior Art***

[20] [21] A patent can be invalid as obvious where the teachings of different prior art references are combined, and there is some suggestion or motivation in the prior art to do so. See ACS Hospital Systems v. Montefiore Hospital, 732 F.2d 1572, 221 U.S.P.Q. 929 (Fed.Cir.1984). However, an invention is not obvious just because all the claimed elements are found in the prior art. There must be something in that prior art to suggest the combination. *See* In re Fritch, 972 F.2d 1260 (Fed.Cir.1992).

In this case, not only does no individual piece of prior art make the "8 patent obvious, there is no combination of references that would make it obvious, and Hercon has not pointed to any suggestion in the prior art that certain elements be combined.

The discussions above for each of the prior art references explain why each does not make the "8 patent obvious. They also explain why it was not obvious to add whatever element was missing from each of these

references. These same reasons lead the court to the conclusion that Hercon has failed to establish by clear and convincing evidence that the combination of elements from several different prior art references would have been obvious at the time of the invention of the "8 patent.

2. *Failure to Disclose Best Mode*

[22] [23] 35 U.S.C. s. 112(1) requires that the specification of a patent "set forth the best mode contemplated by the inventor of carrying out his invention." Determining whether a patent complies with the best mode requirement involves two underlying factual inquiries. Transco Prods, Inc. v. Performance Contracting, Inc., 38 F.3d 551, 559 (Fed.Cir.1994). First, it must be determined whether, at the time the patent application was filed, the inventor had a best mode of practicing the claimed invention. *Id*. If the inventor contemplated such a preferred mode, then what he knew must be compared with what he disclosed to determine whether the disclosure is adequate to enable one skilled in the art to practice the best mode. *Id*. The date for evaluating a best mode disclosure in a continuing application is the date of the earliest application with respect to common subject matter. *Id*. at 557.

[24] Hercon alleges that the inventors of the "8 invention failed to set forth the best mode of practicing that invention because they did not reveal their actual preferred thickness of the adhesive layer. The specification of the "8 patent states that "[t]he thickness [of the adhesive layer] may vary over a wide range but is preferably 2.5 to 5 mm and particularly preferably 3.5 to 4 mm thick." This statement appeared in the original application for the "8 patent. Key contends that the preferred thickness disclosed in the specification is an error, and that "mm" should read "mils." Thus, Key implicitly acknowledges that the inventors had a preferred thickness of 2.5 to 5 mils and a particular preference for a thickness between 3.5 mils and 4 mils at the time of the invention. The court must therefore assess whether what the inventors disclosed in the specification is nevertheless adequate to enable one skilled in the art to practice the best mode.

At trial, Dr. Beasley testified that one of ordinary skill could readily calculate a preferred thickness on the order of about 3 mils from the balance of the information disclosed in the specification. Tr. at 1479-82. In its post-trial briefs, Hercon argues that one of ordinary skill in the art might not necessarily perceive an error in the specification because the thickness actually disclosed would result in an operable system. Hercon does not, however, cite to any evidence that the specification does not adequately disclose to one skilled in the art how to practice the inventors' preferred thickness. Hercon had the burden of proving this fact by clear and convincing evidence. Having failed to do so, Hercon has not established a best mode violation.

D. Inequitable Conduct

Hercon alleges that Key engaged in inequitable conduct by withholding material prior art from the PTO, thereby rendering all claims of the "8 patent unenforceable. *See* Kingsdown Medical Consultants v. Hollister, Inc., 863 F.2d 867, 877 (Fed.Cir.1988) (en banc). Specifically, Hercon alleges that Key withheld the four Japanese Kokais, the GB '990 patent, and the Sablotsky '452 patent.

[25] Patent applicants have a duty to disclose material information to the PTO under the general duty of candor, good faith, and honesty outlined in 37 C.F.R. s. 1.56(a) (1996). Inequitable conduct arises where a patentee fails "to disclose material information during the patent procurement process or [submits] material false information, with the intent to mislead or deceive the patent officer into granting the patent." Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc., 45 F.3d, 1550, 1556-57.

[26] [27] The party alleging inequitable conduct must demonstrate a threshold level of both materiality and intent. Halliburton Co. v. Schlumberger Tech. Corp., 925 F.2d 1435, 1439 (Fed.Cir.1991). If these threshold levels are met, the court balances the actual level of materiality and the actual level of intent, and determines, as a matter of equity, if inequitable conduct has occurred. *Id*. This balancing test should attempt to quantify the amount of materiality and intent, and result in a finding of inequitable conduct where the two sum up to a sufficient level. Critikon, Inc. v. Becton Dickinson, Inc., 120 F.3d 1253 (Fed.Cir.) ("The more material the omission or the misrepresentation, the lower the level of intent required to establish inequitable conduct, and vice versa.").

1. ***Materiality***

[28] [29] The standard for materiality is whether a reasonable examiner would consider the omission or misrepresentation important in deciding whether to issue the application as a patent. Fox Indus., Inc. v. Structural Preservation Sys., Inc., 922 F.2d 801, 803 (Fed.Cir.1990). A reference that is merely cumulative to other references is not material. *Id*.

[30] Key's failure to present to the PTO anything more than the abstracts for the four Japanese Kokais and the DE '400 patent does not satisfy the threshold level of materiality required for an inequitable conduct inquiry.

The abstracts of the Kokais described the basic structure of the patches disclosed in them, and specifically made mention to their cross-linking features. They do not disclose nitroglycerin, which is disclosed in the full translation. However, most of the claims of the "8 patent are not limited to nitroglycerin. The cross-linking feature is the one element from the Japanese Kokais not disclosed in any of the U.S. prior art. Thus the most material elements of the Japanese Kokais were disclosed.

This court has already found that the Japanese Kokais, and the DE '400 patent, do not render the claims of the "8 patent invalid due to obviousness. While the patent applicant's duty to disclose is not limited to prior art that constitutes grounds for invalidity, Fox Indus., 922 F.2d at 803 (standard is whether examiner would consider omission "important"), this is some evidence that the omission was not sufficiently material.

Also, Key did not completely fail to disclose the existence of these foreign patents. The examiner was given the abstracts, and if it appeared to him or her that these patents were particularly relevant, the examiner could have requested full translations of the patents.

Finally, there has been no showing by Hercon that the patent examiner was specifically impressed with some element of the "8 patent that would have been disclosed in the full translations. Critikon, 120 F.3d 1253, 1258 (finding inequitable conduct where applicant did not cite a patent that disclosed a feature upon which "the examiner specifically relied on ... as a point of novelty").

For the same reasons, the submission of the abstract for the DE '400 patent, as opposed to the full GB '990 patent, (its British equivalent), was not a material omission.

The failure by Key to present the PTO with the '452 patent was not a material omission either. The system disclosed in this patent was considered by Key to be a complete failure. *See* Tr. at 180-184; 300. Thus, Hercon has not established that even the threshold level of materiality required before conducting an inequitable conduct balancing test has been met.

2. *Intent*

[31] Hercon has also not established that the threshold level of intent has been met. A finding of simple or gross negligence does not itself justify an inference of intent to deceive. Rather, the involved conduct, viewed in light of all the evidence, including evidence indicative of good faith, must indicate sufficient culpability to require a finding of intent to deceive. Symbol Techs., Inc. v. Opticon, Inc., 935 F.2d 1569, 1582 (1991).

[32] Direct evidence of intent is usually difficult to produce. Critikon, 120 F.3d at 1256. Thus, it is not required where intent can be inferred by surrounding circumstances and review of the record. *Id*. However, the evidence adduced at trial shows a lack of intent by Key and its patent counsel, John Maitner, to mislead or deceive.

[33] Trial evidence shows the following. Although Key did not submit the translations to the PTO at the time that they received them in April 1986, Key's operationswere in disarray due to Schering-Plough's impending acquisition of Key. Tr. at 1730-31.

After Schering-Plough's acquisition of Key, Maitner added the prosecution of the "8 patent application to his heavy workload. By the time he had occasion to first review the "8 patent application there were a significant number of prior art references in its file. Tr. at 930-33. Maitner testified that he did not review each of those references at that time because he "believe[d] the previous attorneys who handled the application had reviewed what they believed was the most relevant art and at that point in time included it in the application." Tr. at 933.

On June 23, 1988, in connection with an amendment to the "8 patent application, Maitner submitted a list of the eight prior art references cited in the PCT search report and copies of the English-language abstracts of the Kokais and the DE '400 patent to the PTO. By this time, Key had obtained a copy of the GB '900 patent, the British counterpart of the DE '400 patent. There is no evidence, however, that Maitner knew at the time that Key had copies of the full English-language translations of the Kokais or the GB '900 patent in its files.

Maitner was apparently aware by December 1988 that Key had in its files copies of the full English-language translations of the Kokais. And at the time he filed a continuation application on December 22, 1988, he was aware that the translations had not been previously submitted to the PTO. As mentioned above, however, the abstracts disclosed the basic structures of the patches, including their cross-linking features.

By at least March 1990, Maitner was aware that Key had a copy of the GB '990 patent in its files. In April 1990, Maitner filed another continuation application but did not cite the GB '990 patent to the PTO. There is no evidence, however, that at that time or any time thereafter Maitner was aware that the patent had not been cited to the PTO.

These are not facts and circumstances from which one can clearly infer a deceitful motive. Hercon produced evidence that Maitner was aware that Key had in its files the full English-language translations of the Kokais and that he knew they had not been submitted to the PTO. However, Hercon produced no evidence that suggests that Maitner did not believe that he had appropriately brought the Kokais to the

attention of the PTO by submitting the abstracts. To the extent that Maitner should have provided the PTO with the full English-language translations of the Kokais, the evidence suggests at most that Maitner was merely remiss in his duties. Such conduct, however, does not justify an inference of deceit.

Having found neither a sufficient level of materiality nor a sufficient level of intent, the court finds that Hercon has not established by clear and convincing evidence that Key's actions constituted inequitable conduct.

III. ***Conclusion***

For the reasons set out above, the court concludes that Hercon has infringed claim 14 of the "8 patent and that Hercon has failed to prove by clear and convincing evidence that the "8 patent is invalid and unenforceable. Key has requested that the court issue an injunction prohibiting Hercon from making, using, offering for sale, selling, or importing any transdermal nitroglycerin patches that infringe claim 14 of the "8 patent, except as provided for by 35 U.S.C. s. 271(e)(1), before the expiration of the "8 patent. To the extent its NTS-FA patches are found to infringe claim 14, Hercon does not challenge Key's entitlement to an injunction so limited in scope. Therefore, the court will grant Key's request.

The court will issue an Order in accordance with this Opinion.