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In Re: Patent Term Extension
Application for
U.S. Patent No. 5,811,447

OCT 16 2015

DENIAL OF PATENT TERM EXTENSION APPLICATION UNDER 35 U.S.C. § 156 FOR U.S. PATENT NO. 5,811,447

This is in response to the information provided in the Response to the Requirement for Information (Response-RFI) regarding the patent term extension application for U.S. Patent No. 5,811,447 (the '447 patent) filed on June 19, 2015. The Response-RFI is in support of an application for extension of the patent term (PTE application) of the '447 patent under 35 U.S.C. § 156 that was filed in the United States Patent and Trademark Office on December 7, 2012. The PTE application was filed by Angiotech Pharmaceuticals Inc. (Applicant), on behalf of Boston Scientific Sciemed, Inc., the patent owner of record. Extension is sought based upon the premarket review under section 515 of the Federal Food, Drug, and Cosmetic Act (FFDCA) of a medical device known by the tradename ZILVER® PTX Drug Eluting Peripheral Stent. The ZILVER® PTX Drug Eluting Peripheral Stent was approved for commercial use and sale by the Food and Drug Administration (FDA) on November 14, 2012.

A determination has been made that the '447 patent is **NOT** eligible for patent term extension under 35 U.S.C. § 156 based upon the regulatory review period of ZILVER® PTX Drug Eluting Peripheral Stent. Therefore, Applicant's PTE application is **DENIED**.

A. PROCEDURAL BACKGROUND

(1) On September 22, 1998, the USPTO issued the '447 patent to Lawrence L. Kunz et al. The '447 patent was originally assigned to NeoRx Corporation.

(2) On November 14, 2012, FDA approved Premarket Approval Application (PMA) No. P100022, thereby granting permission for commercial marketing or use of the ZILVER® PTX Drug Eluting Peripheral Stent.

(3) On December 7, 2012, Applicant filed a PTE Application under 35 U.S.C. § 156(d)(1) to extend the term of the '447 patent based on FDA regulatory review of ZILVER® PTX Drug Eluting Peripheral Stent.

(4) On February 28, 2013, Applicant filed a supplement to its PTE application.

(5) On June 11, 2013, USPTO sent a Requirement for Information to the Applicant pursuant to 37 C.F.R. § 1.750 seeking evidence that Boston Scientific Scimed Inc., through its agent Angiotech Pharmaceutical, was authorized by Cook Medical Technologies, Inc., the marketing

applicant before the FDA, to rely upon the premarket regulatory review activities of Cook Medical Technologies in seeking extension of the '447 patent.

(6) On January 10, 2014, Applicant provided a response to the Requirement for Information including an express authorization from Cook.

(7) On March 13, 2015, pursuant to the Memorandum of Understanding Between the USPTO and the FDA, see 52 Fed. Reg. 17830, May 12, 1987, the USPTO requested assistance from the FDA ("USPTO Letter to FDA") in determining eligibility of the '447 patent for patent term extension based on the regulatory review period of ZILVER® PTX Drug Eluting Peripheral Stent.

(8) On March 23, 2015, USPTO sent a Requirement for Information (RFI) to Applicant seeking information about (1) how the '447 patent claims a method of using the medical device subject to regulatory review under section 515 of the FFDCA, and consequently, (2) whether the amount of paclitaxel present in the ZILVER® PTX Drug Eluting Peripheral stent is administered, "in an amount and for a period of time effective to inhibit the contraction or migration of vascular smooth muscle cells" to achieve the recited "method of biological stenting."

(9) On May 11, 2015, the FDA communicated its findings to the USPTO. The FDA indicated that ZILVER® PTX Drug Eluting Peripheral Stent had been subject to regulatory review under PMA P100022 in accordance with section 515 of the FFDCA, and confirmed that approval of PMA P100022 did represent the first permitted commercial marketing or use of the product subject to regulatory review.

(10) On June 19, 2015, the Applicant timely filed the Response-RFI arguing that at least claim 12 of the '447 patent claims a method of using the approved product.

(11) On June 19, 2015, Applicant timely filed a request for interim extension under 35 U.S.C. § 156(e)(2).

(12) On September 17, 2015, USPTO granted an interim extension for a period of three months from the original expiration date of the '447 patent.

B. DECISION

The USPTO has considered the arguments made by Applicant in the Response-RFI and finds that contrary to the arguments made in the Response-RFI, the '447 patent does not claim a method of using the ZILVER® PTX Drug Eluting Peripheral Stent, the product subject to regulatory review under PMA P100022. Accordingly, the PTE application for the '447 patent is **DENIED**.

I. The '447 patent does not claim the approved product or a method of using the approved product or a method of manufacturing the approved product

35 U.S.C. § 156 states:

> (a) The term of a patent which **claims a product, a method of using a product, or a method of manufacturing a product** shall be extended in accordance with this section from the original expiration date of the patent, which shall include any patent term adjustment granted under section 154(b) if —
>
> (4) the product has been subject to a regulatory review period before its commercial marketing or use. . . .
>
> (f) For purposes of this section:
> (1) The term "**product**" means:
> (A) A drug product.
> (B) Any **medical device**, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act.

(emphases added).

Accordingly, one requirement of the statute is that the patent must claim the approved product, or a method of using or manufacturing the approved product.

In all of the papers filed by the Applicant in support of the PTE application, including the PTE application itself and the Response-RFI, the only claim specifically identified as claiming the approved product, or a method of using or manufacturing the approved product, is claim 12. Claim 12 recites "[a] method of biologically stenting a mammalian blood vessel, which method comprises administering to the blood vessel of a mammal a cytoskeletal inhibitor in an amount and for a period of time effective to inhibit the contraction or migration of the vascular smooth muscle cells."

To be eligible for patent term extension, the patent must claim the "product" or a method of using the "product," or a method of manufacturing the "product" which was subject to the regulatory review. The term product is defined by statute to be, in the context of a review and approval of a PMA, "any medical device." It is self-evident that claim 12, which is directed to a method of biologically stenting a mammalian blood vessel, neither claims a medical device nor a method of manufacturing a medical device. Therefore, the relevant analysis looks at the claim language to determine whether claim 12 of the '447 patent covers a method of using a medical device, *i.e.*, a method of using the ZILVER® PTX Drug Eluting Peripheral Stent.

In this case, the ZILVER® PTX Drug Eluting Peripheral Stent was reviewed and approved under section 515 of the FFDCA and, as such, is a medical device. Clearly Applicant

agrees that the approved product is a medical device since the PTE application described the approved product, the ZILVER® PTX Drug Eluting Peripheral Stent, as "a flexible, slotted tube made of nitinol, *i.e.*, nickel titanium, and coated with paclitaxel." PTE application at page 2. Additionally, the FDA approved labeling (Labeling-attachment 1) for the ZILVER® PTX Drug Eluting Peripheral Stent describes the medical device as:

> The ZILVER PTX-Drug Eluting Peripheral Stent is a self-expanding stent made of nitinol and coated with the drug paclitaxel. It is a flexible, slotted tube that is designed to provide support while maintaining flexibility in the vessel upon deployment. Post-deployment, the stent is designed to impart an outward radial force upon the inner lumen of the vessel, establishing patency in the stented region.

Labeling at 3.

For the '447 patent to claim a method of using the approved product, the method must claim using the ZILVER® PTX Drug Eluting Peripheral Stent. In other words, the claimed method must recite one or more structural elements of the ZILVER® PTX Drug Eluting Peripheral Stent, which is described by applicant as, "a flexible, slotted tube made of nitinol, *i.e.*, nickel titanium, and coated with paclitaxel."

In order to determine whether claim 12 claims a method of using the ZILVER® PTX Drug Eluting Peripheral Stent, it is necessary to look to the written description of the '447 patent to determine the metes and bounds of the method recited in claim 12. The method of use claimed is a method of biological stenting and involves administering to a blood vessel a cytoskeletal inhibitor in an amount and for a period of time effective to inhibit the contraction or migration of vascular smooth muscle cells. The term "biological stenting" is defined in the '447 patent. The written description of the '447 patent states:

> The present invention also provides therapeutic methods and therapeutic dosage forms involving administration of free (i.e., non-targeted or non-binding partner associated) therapeutic agent to target cells. Preferably, the target cells are vascular smooth muscle cells and the therapeutic agent is an inhibitor of vascular smooth muscle cell contraction, allowing the normal hydrostatic pressure to dilate the vascular lumen. Such contraction inhibition may be achieved by actin inhibition, which is preferably achievable and sustainable at a lower dose level than that necessary to inhibit protein synthesis. Consequently, the vascular smooth muscle cells synthesize protein required to repair minor cell trauma and secrete interstitial matrix, thereby facilitating the fixation of the vascular lumen in a dilated state near its maximal systolic diameter. This phenomenon constitutes a **biological stenting** effect that diminishes or prevents the undesirable recoil mechanism that occurs in up to 25% of the angioplasty procedures classified as successful based on an initial post-procedural

angiogram.

'447 patent at column 5, lines 35-53 (emphasis added).

Based on the definition of "biological stenting" in the '447 patent, it is understood that any patency effect is achieved through the targeted administration of an active pharmaceutical agent which inhibits vascular smooth muscle contraction and thereby allows the vessel to remain in a dilated state. In other words, patency is achieved by the active pharmaceutical agent, not through a stent physically implanted into the vessel. Specifically, the '447 patent describes that the "dosage of the therapeutic conjugate may be administered with an infusion catheter to achieve a 10^{-3}M to 10^{-12}M concentration of said therapeutic conjugate at the site of administration in a blood vessel." '447 patent at column 3, lines 55-58. Additionally, the written description identifies other dosage forms which are: "either non-degradable microparticulates or nanoparticulates or biodegradable microparticulates or nanoparticulates. More preferably, the microparticles or nanoparticles are formed of a polymer containing matrix that biodegrades by random, nonenzymatic , hydrolytic scissioning." '447 patent at column 4, lines 19-24. In another embodiment, the written description discusses targeting the administration site by the use of binding proteins/peptides, such as "vascular smooth muscle cell binding protein, tumor cell binding protein and immune system effector cell binding protein." '447 patent at column 5, lines 6-9. Lastly, the written description provides that one embodiment involves administering the therapeutic agent via infusion catheter, and states , "it will be recognized that other methods for drug delivery or routes of administration may also be useful, e.g., injection by the intravenous, intralymphatic, intrathecal, intraarterial, local delivery by implanted osmotic pumps or other intracavity routes." '447 patent at column 31, lines 1-5.

Not a single disclosed embodiment or any written description involves implanting a nitinol stent structure containing a drug component into a vessel to achieve the claimed method of "biological stenting." In fact, the only instance in which the term stent is used in the '447 patent, outside of the term "biological stenting," is in reference to the patient population that may benefit from the method of the claim 12. Specifically, the written description states:

> In a preferred aspect, the infusion catheter may be conveniently a double balloon or quadruple balloon catheter with a permeable membrane. In one representative embodiment, a therapeutically effective dosage of a therapeutic conjugate or dosage form is useful in treating vascular trauma resulting from disease (e.g., atherosclerosis, aneurysm, or the like) or vascular surgical procedures such as angioplasty, atheroectomy, placement of a stent (e.g., in a vessel), thrombectomy, and grafting.

'447 patent at column 30, lines 36-44.

In the RFI dated March 25, 2015, the USPTO required the Applicant to describe "how the '447 patent claims a method of using the medical device subject to regulatory review under

section 515 of the FFDCA." In response, Applicant asserts that the '447 patent claims a method of using the ZILVER® PTX Drug Eluting Peripheral Stent. Response-RFI at page 5. Specifically, Applicant states that the FDA Summary of Safety and Effectiveness Data (SSED) indicates that the ZILVER® PTX Drug Eluting Peripheral Stent can be used in a method for:

> biologically stenting a mammalian blood vessel **[with an implantable blood-contacting device]**, which method comprises administering to the blood vessel of a mammal a cytoskeletal inhibitor **[by inserting the ZILVER PTX Drug Eluting Peripheral Stent, coated on its outer surface with the cytoskeletal inhibitor paclitaxel,]** in an amount and for a period of time effective to inhibit the contraction or migration of the vascular smooth muscle cells . . . .

Response-RFI at 4-5 (emphases added). The USPTO finds that claim 12 of the '447 patent does not claim a method of using the ZILVER® PTX Drug Eluting Peripheral Stent. The bracketed language in the above reproduced language from claim 12 of the '447 patent is not actually found in the express language of claim 12, nor found anywhere in the written description of the '447 patent. Thus, the USPTO does not agree with Applicant's statement that the '447 patent claims a method of using the medical device subject to regulatory review under section 515 of the FFDCA. To the contrary, as discussed above, there is no claim language indicating that the claimed method uses the approved product, the ZILVER® PTX Drug Eluting Peripheral Stent, and there is no written description in the '447 patent indicating that a mode of administration of the "cytoskeletal inhibitor" is via a drug-coated stent.

Turning to the express language of claim 12, USPTO finds that the claim contains no recitation of a physical structure that is "a flexible slotted tube made of nitinol, i.e., nickel titanium, and coated with paclitaxel." Instead, claim 12 of the '447 patent is directed to a method for biological stenting by administering to the blood vessel a cytoskeletal inhibitor.

Also in the RFI, the USPTO required Applicant to describe whether the amount of paclitaxel present in the ZILVER® PTX Drug Eluting Peripheral stent is administered, 'in an amount and for a period of time effective to inhibit the contraction or migration of vascular smooth muscle cells' to achieve the recited 'method of biological stenting.'"

Applicant states in the Response-RFI that the "primary patency rate at 12 months was 90.2% for the Zilver PTX stent compared to 72.9% for the bare Zilver stent." Response-RFI at 5. Applicant concludes that this determination of the patency rate at 12 months is evidence that the paclitaxel coating is present "in an amount and for a period of time effective . . . to achieve the recited 'method of biological stenting.'" *Id.* Regardless of whether paclitaxel achieves biological stenting, this information does not support a conclusion that claim 12 claims a method of using the ZILVER® PTX Drug Eluting Peripheral Stent. At most, this information might support a conclusion that claim 12 claims a method of using paclitaxel as a cytoskeletal inhibitor. Moreover, the information from the SSED that discusses the patency effect shows that placement of a physical stent into a vessel achieves some level of patency. That is, patency is achieved

whether or not a cytoskeletal inhibitor (paclitaxel) is included in the stent system. But in the '447 patent, patency is achieved by the active pharmaceutical agent alone (*i.e.*, "biological stenting), rather than by a physical stent.

The analysis provided in the Response-RFI does not provide a persuasive answer to either question specifically asked by the USPTO in the RFI of March 23, 2015. Claim 12 may cover the administration of paclitaxel to achieve "biological stenting" through the recitation of "administering to the blood vessel of a mammal a cytoskeletal inhibitor." However, as pointed out, the approved product is a medical device and, contrary to Applicant's remarks in the Response-RFI, claim 12 of the '447 patent does not claim a medical device, a method of using a medical device, or a method of manufacturing a medical device. Applicant concludes that "[t]he above chart shows that each and every element of claim 12 is present in the ZILVER® PTX Drug Eluting Peripheral Stent, as set forth in the SSED." Response-RFI at 4. Although the chart may show that the ZILVER® PTX Drug Eluting Peripheral Stent could be used to deliver paclitaxel to the blood vessel of a mammal, the chart does not show that claim 12 of the '447 patent claims the ZILVER® PTX Drug Eluting Peripheral Stent, a method of using the ZILVER® PTX Drug Eluting Peripheral Stent, or a method of manufacturing the ZILVER® PTX Drug Eluting Peripheral Stent. As the Federal Circuit stated in *Hoechst-Roussel Pharamceuticals Inc. v. Lehman*, 109 F.3d 756, 759, 42 U.S.P.Q.2d 1220 (Fed. Cir. 1997), "the concept of a 'claim' is different from the concept of infringement, and, as a result, the plain meaning of 'claims' is not the same as the plain meaning of infringement." Here, it appears that Applicant has conflated the concept of claiming a method of using the product (the medical device which was subject to regulatory review) with whether making, using, offering to sell, or selling the ZILVER® PTX Drug Eluting Peripheral Stent would, in theory, infringe claim 12 of the '447 patent. The Federal Circuit has expressly rejected the argument that an FDA-approved product that would infringe a claim is also necessarily "claimed" (for purposes of 35 U.S.C. § 156) in that claim. *Hoechst-Roussel*, 109 F.3d at 758.

It appears that Applicant construes claim 12 as covering every conceivable way of administering a cytoskeletal inhibitor to a mammalian blood vessel. But the written description of the '447 patent does not support such a broad reading of claim 12. As noted above, there is no disclosure in the '447 patent indicating that a mode of administration of the cytoskeletal inhibitor is via a drug-coated stent. Thus, the specification does not convey to a skilled artisan that the inventors of the '447 patent actually invented (or had possession of) a method of using "a flexible, slotted tube made of nitinol . . . coated with paclitaxel" and could claim the same. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (*en banc*).

C. CONCLUSION

Thus, for the reasons above, the USPTO finds that claim 12 of the '447 patent does not cover a method of using the ZILVER® PTX Drug Eluting Peripheral Stent. As such, the application for term extension of the '447 patent is **DENIED** as failing to comply with 35 U.S.C. 156(a), because no claim of the '447 patent claims the approved product, a method of using the

approved product or a method of manufacturing the approved product.

This is a final agency action within the meaning of 5 U.S.C. 704 for purposes of seeking judicial review.

Any correspondence from applicant with respect to this matter should be submitted via the USPTO's EFS Web system and should be addressed as follows:

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Alexandria, VA 22313-1450.

Telephone inquiries related to this determination should be directed to Mary C. Till at (571) 272-7755.

Brian E. Hanlon

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cc: FDA, CDER, Office of Regulatory Policy
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Attention: Beverly Friedman

RE: ZILVER® PTX Drug
Eluting Peripheral Stent
Docket No.: FDA-2013-E-0781