# In the United States Patent and Trademark Office

In re United States Patent No: 6,869,939

U.S. Application No.: 10/139,620

Filed: May 4, 2002

Granted: March 22, 2005

Patentees: Gerold L. MOSHER *et al.*

Assignee: Cydex, Inc.

For: Formulations Containing Amiodarone and Sulfoalkyl Ether Cyclodextrin

## Request for Reconsideration of Final Determination of Ineligibility

**Mail Stop: HATCH WAXMAN-PTE**

Sir:

This is a Request for Reconsideration of the decision in the Notice of Final Determination – Ineligible, mailed March 16, 2010, by the U.S. Patent and Trademark Office (hereinafter "Notice"). The Notice was issued in connection with an Application for Patent Term Extension Pursuant to 35 U.S.C. § 156 filed in the above-captioned patent on February 17, 2009 (hereinafter "PTE Application"). A Request for Reconsideration of the Final Determination of Ineligibility may be filed within two months of the mailing date of the Notice (*i.e.,* by May 16, 2010). Thus, this Request for Reconsideration is being timely filed.

According to the Notice, U.S. Patent No. 6,869,939 (hereinafter "the '939 patent") is not eligible for patent term extension under 35 U.S.C. § 156 based on the regulatory review period of NEXTERONE®. The Notice states that "the December 24, 2008 approval of NEXTERONE®

(amiodarone hydrochloride) does not constitute the first permitted commercial marketing or use of the 'product' under section 505 of the FFDCA [Federal Food Drug and Cosmetic Act]." (*See* Notice at page 1). The Notice further states "the PTE Application does not satisfy the requirement of section 156(a)(5)(A) and the '939 patent is ineligible for a patent term extension. Thus, the PTE Application must be dismissed." (*Id.* at page 3).

In response, reconsideration is requested on the grounds that NEXTERONE® represents the first permitted commercial marketing or use of the Nexterone "product," sulfobutyl ether β-cyclodextrin-amiodarone hydrochloride complex, as defined in 35 U.S.C. § 156(f)(1) and (2).

The term "product" as used in section 156(a)(5)(A) is defined in section 156(f)(1) as "drug product," and the term "drug product" is defined in section 156(f)(2) as the "active ingredient of a new drug, antibiotic drug, or human biological product . . . including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient." 35 U.S.C. § 156(f)(2)(A)-(B).

The Notice has interpreted the statements made in the PTE Application to mean that the active ingredient in the drug product NEXTERONE® is limited to amiodarone hydrochloride.

According to the Notice:

> It is undisputed that amiodarone hydrochloride is the active ingredient of Applicant's NEXTERONE® drug product. In response to the requirement of 37 C.F.R. § 1.740(a)(4) to identify each active ingredient in the product, the PTE Application identifies one and only one active ingredient. Specifically, the PTE Application at page 5 identifies amiodarone hydrochloride as "[t]he active ingredient of the product NEXTERONE®." This is consistent with results from a Detail Record Search for NEXTERONE® in the electronic Orange Book, as accessed on March 20, 2009 (a copy of the printout is attached), which also identifies amiodarone hydrochloride as the sole active ingredient of NEXTERONE®. It is also consistent with the FDA's September 30, 2009 letter to the USPTO.

(*See* Notice at page 2).

The PTE Application states that "[t]he active ingredient of the product NEXTERONE® (amiodarone hydrochloride) Injection is amiodarone hydrochloride." (S*ee* PTE Application at page 5.) However, the PTE Application further states that the drug product is "sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex." (*Id.*). The identification of "amiodarone hydrochloride" on page 5 of the PTE Application was simply to indicate that amiodarone

hydrochloride provides the pharmacological activity of the drug product. It was the intention of Applicants to convey that the "active ingredient" in the drug product NEXTERONE® is the sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex.

The term "active ingredient" is defined in 37 C.F.R. § 60.3(b)(2), for purposes of the Food and Drug Administration's (FDA's) analysis of Requests for Patent Term Restoration (Extension) as:

> Active ingredient means any component that is intended to furnish *pharmacological activity* or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure of any function of the body of man or of animals. *The term includes those components that may* undergo chemical change in the manufacture of the drug product and *be present in the drug product in a modified form intended to furnish the specified activity or effect.*

37 C.F.R. § 60.3(b)(2) (emphasis added).

The definition of "active ingredient" clearly includes components that are "present in the drug product in a modified form intended to furnish the specified activity or effect." *Id.* As discussed throughout the '939 patent, amiodarone forms an inclusion complex with sulfobutyl ether-β cyclodextrin. The '939 patent further describes the interaction between amiodarone and sulfobutyl ether-β cyclodextrin resulting in a complex in which the amiodarone is "part of a clathrate or inclusion complex." *See* the '939 patent at column 14, line 65 through column 15, line 1. Thus, sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex is the "active ingredient" of NEXTERONE®.

The complex between sulfobutyl ether β-cyclodextrin and amiodarone hydrochloride results from interactions between the hydrophobic portions of sulfobutyl ether β-cyclodextrin and amiodarone. As set forth in the '939 patent:

> In aqueous solutions, these hydrophobic cavities provide a haven for hydrophobic organic compounds, which can fit all, or part of their structure into these cavities. This process, known as inclusion complexation, may result in increased apparent aqueous solubility and stability for the complexed drug. The complex is stabilized by hydrophobic interactions and does not involve the formation of any covalent bonds.

(*See* the '939 patent at column 3, lines 58-65).

As discussed throughout the '939 patent, the sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex provides a pharmaceutically stable formulation that can be diluted in a wide range of buffers without requiring a surfactant in order to render it suitable for dilution. (*See e.g.*, the '939 patent at column 8, lines 1-15). It is this complex that "provides significant advantages over other cyclodextrin-containing formulations of amiodarone." (*See* the '939 patent at Abstract, and throughout columns 16-17).

The definition of "active ingredient" noted above specifically includes *components* of a drug product that serve to provide *pharmacological activity*, as well as *components intended to furnish the specified activity or effect*. The term "active ingredient" therefore applies to sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex, and thus it is this complex that is the drug product, as defined in 35 U.S.C. § 156(f)(2).

The Notice incorrectly asserts that the facts of the present case are completely analogous to those in *Fisons plc v. Quigg*, 876 F.2d 99 (Fed. Cir. 1989).

> Just as it is undisputed here that amiodarone hydrochloride is the active ingredient of Applicant's NEXTERONE® drug product, it was undisputed in the *Fisons* cases that cromolyn sodium was the active ingredient of the products at issue in the *Fisons* cases.

(*See* Notice at page 3).

While amiodarone hydrochloride may provide the *pharmacological activity* of the drug product, the active ingredient of NEXTERONE® is the sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex. Thus, the present facts are not analogous to those in *Fisons*. In *Fisons*, the patents and products seeking patent term extension represented "an innovative *use* or *dosage form* of cromolyn sodium." *Fisons*, 876 F.2d at 100 (emphasis added). In contrast, the PTE Application for the '939 patent covering NEXTERONE® is for a new *active ingredient*, namely sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex, not a new use or dosage form, as in *Fisons*.

The Notice also cites *In re Alcon Labs*, 13 USPQ2d 1115 (Comm'r of Pats. 1989) and *Arnold Partnership v. Dudas*, 362 F.2d 1338 (Fed. Cir. 2004), as support for the "Office's long-standing position that if a drug product contains two active ingredients, each of which has been previously approved individually, then regulatory approval of the combination drug product

cannot be the basis for extension of a patent claiming the approved combination." (*See* Notice at page 4).

While *In re Alcon Labs* and *Arnold Partnership* may in fact support this position, these facts are inapplicable to the present case. As discussed above, NEXTERONE® does not contain two active ingredients, but rather a single active ingredient, the sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex. This drug product was not previously approved by the FDA. The fact that amiodarone hydrochloride may have been previously approved, and additional previous combination products comprising sulfobutyl ether β-cyclodextrin may have also been approved, should not render the '939 patent covering NEXTERONE® ineligible for patent term extension.

In view of the foregoing remarks and contrary to the assertions in the Notice, the "drug product" for which patent term extension is being sought is sulfobutyl ether β-cyclodextrin amiodarone hydrochloride complex (*i.e.,* NEXTERONE®). As discussed throughout the PTE Application, this is the first permitted commercial marketing for this drug product. The remaining requirements under 35 U.S.C. § 156 are also clearly met for NEXTERONE®, as set forth in the PTE Application. Thus, reconsideration of the Notice, and granting of the requested patent term extension of the '939 patent, are respectfully requested.

It is not believed that extensions of time or fees beyond those that may otherwise be provided for in documents accompanying this paper are required. However, if additional extensions of time are necessary, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. 50-5071.

Please direct all inquiries and correspondence relating to this Request for Reconsideration of patent term extension to the registered practitioner identified below acting on behalf of the patent owner.

Respectfully submitted,

Date: May 11, 2010 *By*: /Dean L. Fanelli/

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