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Dockets Management Branch
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CITIZEN PETITION

Pfizer Inc ("Pfizer") submits this petition under 21 C.F.R. 10.30 to request that the Food and Drug Administration ("FDA"):

1. Revoke the approval of the Allergan Inc. supplemental New Drug Application #21-275/S-013 ("Allergan sNDA") for a first-line indication for Lumigan® (bimatoprost ophthalmic solution 0.03%).

2. Deny approval for the Alcon Inc. supplemental New Drug Application #21-257 ("Alcon sNDA") for a first-line indication for Travatan® (travoprost ophthalmic solution 0.004%).

Both sNDAs were filed under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act ("FFDCA") and reference the supplemental New Drug Application ("sNDA") for Pfizer's listed drug Xalatan® (latanoprost ophthalmic solution 0.005%).

ACTIONS REQUESTED

Pfizer requests that FDA revoke the approval of the Allergan sNDA for a first-line indication and deny approval of the Alcon sNDA for a first-line indication. As set forth herein, Pfizer submits that approval of the Allergan and Alcon sNDAs is inappropriate and unlawful because:

1. FDA does not have authority under section 505(b)(2) to approve the Allergan or Alcon sNDA based on confidential, non-public information contained in the Xalatan NDA; any such reliance on the Xalatan NDA information would constitute a "taking" and a violation of trade secrets;

2. Even if FDA were authorized to rely on the Xalatan NDA (it is not), the data and information in the Xalatan NDA do not provide substantial evidence establishing that Lumigan or Travatan is appropriate for first-line use as the drugs have distinct structures, concentrations and safety profiles; and

3. It would be arbitrary and capricious for FDA to approve Lumigan or Travatan as first-line therapies in the absence of clinical data substantiating the safety of those products for first-line use, when FDA required Pfizer, in closely similar circumstances, to submit significant additional data in order to obtain a first-line indication for Xalatan.

STATEMENT OF GROUNDS

BACKGROUND

A. Xalatan Approved for First-Line Indication

1. Xalatan NDA

Xalatan is a prostaglandin[1] derivative called latanoprost and is sold in a 0.005% solution. FDA approved Xalatan in 1996 (NDA #20-597) as a second-line agent for the treatment of elevated intraocular pressure ("IOP") in patients with open-angle glaucoma and/or ocular hypertension. At that time, Xalatan was not approved as a first-line agent primarily due to the need for more information about long-term safety.

2. First-Line Indication Approved for Xalatan in 2002 after Submission of Significant Additional Safety Data over a 3-year Period

On June 30, 1999, Pfizer submitted a sNDA (#S-010) seeking to expand the indication for Xalatan to a *first-line* treatment for open-angle glaucoma and ocular hypertension. FDA initially responded to this request with a "not approvable" letter dated October 20, 1999. FDA stated that the information presented in the application was inadequate and outlined four issues that would need to be addressed before Xalatan could be approved as a first-line treatment. These included concerns about the long-term safety consequences associated with the use of Xalatan, such as the potential for iris pigmentation changes, growth of eyelashes and other ocular structures, and the risk of cystoid macular edema in aphakic and pseudophakic patients.

In response to FDA's requests, Pfizer conducted extensive long-term pharmacovigilance and postmarketing studies, as well a series of extensive investigations that included nonclinical *in vivo* and *in vitro* studies using animal and human specimens. Among these were:

- A 5-year long-term safety study of 344 patients;

[1] Prostaglandins are a series of naturally occurring fatty acids found throughout the body.

- A 5-year, comprehensive post-marketing surveillance study involving 5000 patients;
- Morphological examinations of trabeculectomy specimens taken from patients treated with latanoprost for up to 41 months;
- A study of melanin in the trabecular meshwork of latanoprost patients; and
- Five years of post marketing experience during which time approximately 17 million patients were treated with latanoprost.

On December 20, 2002, FDA approved Xalatan for first-line use. In recognition of Pfizer's research efforts, FDA granted Pfizer three years of market exclusivity pursuant to section 505(c)(3)(E) of the FFDCA.

B. Lumigan and Travatan Supplemental NDAs filed under Section 505(b)(2)

In 2001, FDA approved Lumigan and Travatan for second-line treatment of elevated IOP in open-angle glaucoma or ocular hypertension. In 2006, Allergan and Alcon filed sNDAs seeking approval for first-line indications for Lumigan and Travatan. Pfizer received patent certification notices indicating that both sNDAs were submitted under Section 505(b)(2) of the FFDCA, referencing Xalatan.

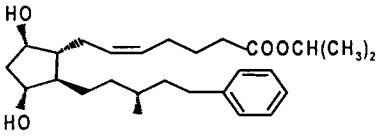
On June 23, 2006, Allergan announced that FDA had approved Lumigan for first-line use. Alcon's 505(b)(2) application for a first-line indication is currently being reviewed by FDA. It is Pfizer's understanding that FDA is relying on the data and information that Pfizer submitted in a sNDA to FDA to gain approval of Xalatan for first-line use.

C. Differences between Latanoprost, Bimatoprost, and Travoprost

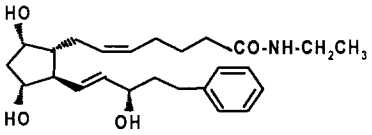
1. Latanoprost, Bimatoprost and Travoprost are Distinct Molecules

Although the active ingredients found in Xalatan, Lumigan and Travatan –latanoprost, bimatoprost and travoprost respectively – are related, they are not the same. Latanoprost and travaprost are prostaglandins. Bimatoprost, as it is identified in the Lumigan NDA and package insert, is a "prostamide"— a classification that Allergan itself claims is distinct from prostaglandins. While the significance of the prostamide-prostaglandin category is the subject of some debate, it is certainly the case that the three molecules have different structures and are formulated with different concentrations. These differences have significant impact on safety (Stjernschantz 2004) as discussed in more detail below.

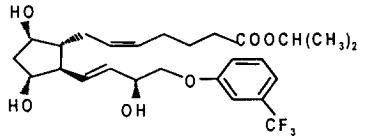
a. *Molecular Structures*



Xalatan (latanoprost ophthalmic solution), isopropyl ester



Lumigan (bimatoprost ophthalmic solution) , N-ethyl amide



Travoprost (travoprost ophthalmic solution), isopropyl ester

Difference in Carbon Bonds. In the latanoprost molecule, the double bond between C 13 and 14 has been saturated, creating a single bond between C13 and 14. In contrast, bimatoprost and travoprost both have a double bond between carbons 13 and 14.In the development of latanoprost, it was found that the saturation of the 13-14 double bond actually increased therapeutic index and chemical stability (Stjernschantz 2001). The saturation of the double bond in latanoprost results in an improvement in its receptor profile (Stjernschantz 2001). Further, there is evidence that the saturated double bond tends to reduce the hyperemic effect as compared to an intact double bond (Stjernschantz 2004; Stjernschantz, 2001).

Difference in Omega Chain. Another significant difference in the molecular structures relates to the omega chain: unlike latanoprost, travoprost has a substitution on the phenyl ring.

As discussed in more detail below, these chemical differences translate into several important clinical differences and result in distinct side effects among the three products.

b. Concentrations

Bimatoprost and travoprost are used at significantly higher concentrations than latanoprost. Travoprost and bimatoprost are used at significantly higher concentrations than latanoprost when taking into consideration their pharmacological potency. However, the IOP reducing effects of the three drugs are all very similar (Netland 2001; Noecker 2003; Parrish 2003).

Travoprost is claimed to be around 10 times more potent than latanoprost in biochemical tests (Hellberg 2002; Stjernschantz 2001), yet the IOP reduction is practically the same as latanoprost (Parrish 2003; Netland 2001; Noecker 2003). Similarly, the concentration of bimatoprost is 0.03%, nearly 6 times the concentration of latanoprost. The increased drug concentrations of Lumigan and Travatan, relative to Xalatan, may contribute to the higher rates of ocular side effects seen with these drugs. (*See* Lumigan and Travatan Package Inserts).

Further, unlike latanoprost and travoprost, bimatoprost acquires its lipophilic character through derivatization of C-1 as an ethyl amide, rather than an isopropyl ester (Maxey 2002). Thus, bimatoprost is an N-ethyl amide, while latanoprost is an isopropyl ester. There is evidence suggesting that because bimatoprost is a prostamide, it is more difficult for the drug to penetrate the eye due to poor corneal penetration, necessitating a high concentration of bimatoprost in Lumigan. (Maxey 2002; Eisenberg 2002, 2003).

2. Safety Differences Exist Between Latanoprost, Bimatoprost and Travoprost

As discussed above, latanoprost, bimatoprost and travoprost have different chemical structures and are used in different concentrations. These differences have important clinical implications, and result in significantly different safety profiles with respect to rates and intensity of hyperemia, eyelash changes, and rates of lid sulcus deepening (Stjernschantz 2001).

Hyperemia. Significant differences in conjunctival hyperemia incidence and intensity have been observed among prostaglandins (and prostamides) in comparative trials. In these trials, both travoprost and bimatoprost produced significantly higher rates of hyperemia than latanoprost. For example, in two separate trials sponsored by Allergan (Gandolfi 2001; Noecker 2003), hyperemia occurred significantly more frequently with bimatoprost (36.1% and 44%) compared to latanoprost (14.2% and 20%, respectively). Similarly, in a controlled clinical trial sponsored by Alcon (Netland 2001; Parrish 2003), travoprost had a significantly higher rate of hyperemia than latanoprost (49.5% vs. 27.6%). The package inserts for each of the prostaglandins indicate that travoprost and bimatoprost have relatively higher rates of hyperemia than does latanoprost. It is unknown whether exposure to sustained hyperemia long-term will result in increased morbidity.

Eyelash Changes. Significantly higher rates of eyelash changes (including length, thickness, density, and color) have been reported (including studies sponsored by Allergan) with bimatoprost (10.5%) as compared to latanoprost (0%) in comparative trials (Gandolfi 2001, Noecker 2003). Similarly, significantly higher rates of eyelash changes were observed with travoprost (57.1%) than latanoprost (25.8%) in studies sponsored by Alcon (Netland 2001).

Eyelid Sulcus. Differences have been reported among prostaglandins in the incidence and in the dose required to produce palpebral fissure ("PF") and/or deepening of the lid sulcus. Generally, higher rates of periocular sulci and PF were observed with both travoprost and bimatoprost compared to latanoprost in both animal models and humans. (Package Inserts, CDER Pharmacology Review NDA #21-257 (travaprost), page 24; CDER Pharmacology Review NDA #21-274 (bimatoprost), page 68.) Additionally, there have been numerous reports of possible postmarketing patient complications of bimatoprost therapy related to lid sulcus from bimatoprost (Peplinski 2004).

3. Distinct Long Term Safety and Efficacy Profiles

In 2002, Xalatan was the only drug in the prostaglandin therapeutic class granted a first-line indication, reflecting FDA's recognition that there are distinctions among prostaglandins and prostamides that may result in significant qualitative and quantitative differences in long-term safety. Extensive data and information demonstrating the safety of latanoprost were part of the Pfizer sNDA for a first-line indication.[2] Among other things, Pfizer conducted a 5 years post-marketing safety study (over 5,000 patients enrolled) which demonstrated new onset iridial pigmentation did not occur between 3 and 5 year of treatment. Neither bimatoprost nor travoprost has demonstrated this long-term safety for patients. Additionally, although reduction of IOP was not a primary endpoint for this study, it was clearly demonstrated that IOP was reduced and this reduction was maintained at 5 years in those patients who were treated with latanoprost. To date, neither bimatoprost nor travoprost can claim this same extent of efficacy (5 years).

[2] In its initial "not approvable" response to the Xalatan sNDA for a first-line indication, FDA indicated that it had concerns about "potential safety issues related to increasing ocular pigmentation and growth of ocular structures." Letter from FDA re NDA 20-597/S-010 to Pharmacia Corporation, October 9, 2001.

DISCUSSION

Pfizer submits that, for the following reasons, it is unlawful and scientifically unjustified for FDA to grant first-line indications to Lumigan and Travatan on the basis of studies that Pfizer conducted on Xalatan. Thus, Pfizer requests that FDA withdraw its approval of the Allergan sNDA, and deny approval of the Alcon sNDA, if those approvals are predicated on data regarding Xalatan that Pfizer submitted confidentially to the Xalatan NDA.

A. FDA Has No Legal Authority To Approve the Allergan and Alcon sNDAs Based on Confidential Data in the Xalatan NDA

In prior Citizen Petitions,[3] which are incorporated by reference herein (See Appendix A), Pfizer demonstrated that FDA does not have the authority to rely on confidential, unpublished data in an innovator's NDA in order to approve a third-party's Section 505(b)(2) NDA. As outlined in these prior Citizen Petitions, Section 505(b)(2) authorizes only the use of *publicly available* reports of investigations to satisfy the "full investigations" requirements for applications submitted under Section 505(b). Congress did not intend, nor does the language of Section 505(b)(2) indicate, that a 505(b)(2) application may rely on *non-public* proprietary data in an NDA. Such reliance is authorized only for Abbreviated New Drug Applications ("ANDAs") filed under Section 505(j) of the FFDCA.

Further, Pfizer takes issue with FDA's position that reliance on prior FDA "findings" negates the problem of inappropriate reliance on confidential, unpublished data and information.[4] Pfizer articulated this argument in a prior filing[5], which is incorporated by reference here, and is attached as Appendix B. In brief, any reliance by FDA on prior "findings" about a drug is equivalent to reliance on data contained in the NDA on which those findings were based. This equivalence is reflected in numerous court opinions that describe the generic drug approval process interchangeably as allowing FDA to rely on pioneer data or on Agency "findings" based on those data.[6]

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[3] Pfizer Citizen Petition (Requesting that FDA reject Omnitrope 505(b)(2) application), Docket No. 2004P-0231, May 13, 2004; Pfizer Citizen Petition, Docket No. 02P-0447, October 11, 2002 (Requesting *inter alia* that FDA deny approval of Dr. Reddy's NDA for amlodipine maleate tablets under section 505(b)(2) of the FFDCA if that NDA relies on any non-public proprietary data in Pfizer's NDA for Norvasc); Pfizer Citizen Petition, Docket No. 01P-0323, July 27, 2001 (Requesting *inter alia* that FDA not rely on or otherwise use non-public proprietary information in an innovator's NDA or other non-public filings to approve section 505(b)(2) applications,.

[4] FDA Response to Pfizer Citizen Petition and BIO Citizen Petition, Dockets Nos. 2001P-0323/CP1 & C5, 2002P-0447/CP1, October 14, 2003.

[5] Pfizer Reply to Comments of Dr. Reddy's Laboratories, Docket No. 02P-0447, April 28, 2003; included as Appendix B.

[6] For example, the D.C. Circuit has interchangeably characterized an ANDA as "relying on the NDA filed by the original manufacturer," *American Bioscience, Inc. v. Thompson*, 243 F.3d 579, 580 (D.C. Cir 2001); *Bristol Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1495 (D.C. Cir. 1996) ("The principal advantage of securing approval [by an ANDA] is that the applicant may rely upon research paid for by the manufacturer of the listed drug), and is an application, "which relies on the FDA's previous determination that the drug is safe and effective . . ." *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1063 (D.C. Cir. 1998); *see Andrx*

As outlined above, the Allergan and Alcon sNDAs appear to rely upon the safety data Pfizer submitted confidentially in order to gain approval for a first-line indication for Xalatan. FDA has no authority, however, to use those data without Pfizer's consent for the benefit of a third party. Any reliance by FDA on this confidential, non-public information in the Xalatan NDA in order to approve the Allergan or Alcon sNDA, is unlawful.

Further, any FDA reliance on data and information in the Xalatan NDA constitutes a "taking" and a violation of trade secrets. As outlined in more detail in a prior Citizen Petition,[7] the United States Constitution prohibits the government from taking protected property without providing just compensation and prior due process,[8] and FDA's regulations protecting innovators' manufacturing information as trade secrets creates a "reasonable investment-based expectations" that such information is protected under the Fifth Amendment.[9] An inherent property right in safety and effectiveness data submitted as part of an NDA has long been recognized by the courts and FDA.[10] Accordingly, unauthorized release or use of a manufacturer's trade secrets constitutes a taking under the Fifth Amendment.[11]

Pharm, Inc.v. Biovail Corp., 256 F.3d 799, 801 (D.C. Cir. 2001) (ANDA "relies on the FDA's previous determination that the drug is safe and effective," *cert denied*, 533 U.S. 931 (2002)). As illustrated by the courts alternating use of these terms, the D.C. Circuit has recognized that reliance on NDA data is equivalent to reliance on FDA's previous findings of safety and effectiveness based upon that data. The court is simply using different terminology to describe what is plainly the same thing.

[7] *See* Citizen Petition from Pfizer Inc to FDA, Docket No. 01P-0323, July 27, 2001; included in Appendix A.

[8] U.S. Const. Amend. V, XIV.

[9] *PruneYard Shopping Center v. Robins,* 447 U.S. 74, 83 (1980); *Ruckelshaus v. Monsanto Co.,* 467 U.S. 986, 1011 (1984).

[10] *See, e.g., Serono Laboratories v. Shalala*, 35 F. Supp. 2d 1(D.D.C. 1999)(denying in part a discovery motion seeking production from FDA of the administrative record underlying approval of an ANDA on grounds that some of the information was protected and not eligible for disclosure because it was trade secret); *A.L. Labs Inc. v. Philips Roxane, Inc.*, 803 F.2d 378, 383-85 (8th Cir. 1986) (upholding punitive damages and injunction against manufacturer because manufacturer had relied on an innovator's data without authorization to obtain approval of an animal drug application); *Anderson v. Department of Health and Human Services*, 907 F.2d 936 (10th Cir. 1990) ("[M]anufacturing and processing information, including formulations, chemistry and quality assurance procedures" are within the definition of trade secrets; the majority of information in an IND, NDA, and IDE are likely trade secrets); *Public Citizen Health Research Group*, 997 F. Supp. 56, 62 (D.D.C. 1998) (safety and effectiveness information about a manufacturer's drug may be of great assistance to competing drug manufacturers – the release of the types of data and information in NDA and IND files constitute "substantial commercial harm").

FDA has also recognized the protected rights in clinical NDA data, 21 C.F.R. 314.50(g) and has regulations to protect trade secret and confidential information in drug marketing applications. 21 C.F.R. 20.21; 21 C.F.R. 20.61; 21 C.F.R. 31.430(e)(3); and 21 C.F.R. 3314.430(g)(1).

[11] In addition, under longstanding case law, FDA would be required to provide a manufacturer with notice, a hearing, and an opportunity for judicial review before releasing any trade secret data. *American Sumatra Tobacco Corp. v. SEC*, 93 F.2d 236, 239 (D.C. Cir. 1937).

B. Even If Reliance on the Xalatan NDA Were Permissible (It Is Not), Such Reliance Is Not Scientifically Justified And May Put Patient Safety at Risk

Even if FDA had the legal authority to approve the Allergan and Alcon sNDAs under Section 505(b)(2) in reliance on Pfizer's Xalatan data (as explained above, FDA does not have that authority), such reliance is scientifically unjustified.

In its decision earlier this year to approve a Section 505(b)(2) application for a somatropin product (over Pfizer's objection), FDA asserted that under Section 505(b)(2) it would rely on prior findings from NDA data only to the extent that "the proposed product in the 505(b)(2) application shares characteristics (*e.g.*, active ingredient, dosage form, strength, route of administration, indication, conditions of use) in common with the listed drug," such that the products may be regarded as "substantially similar." Letter from FDA to Kathleen M. Sanzo, Esq., Stephan E. Lawton, Esq., and Stephen G. Juelsgaard, Esq., Docket Nos. 2004P-0231/CP1 and SUP1, 2003P-0176/CP1 and EMC1 2004P-0171/CP1 and 2004N-0355, May 30, 2006. The Allergan and Alcon sNDAs clearly do not satisfy this standard, because the Allergan and Alcon products, bimatoprost and travoprost, are molecularly distinct compared with latanoprost, have distinct molecular structures and concentrations used to effect IOP lowering, and have significant safety/side effect differences in rates of hyperemia, eyelash changes and eyelid sulcus.

In light of these differences, and under FDA's own interpretation of 505(b)(2), FDA cannot reasonably approve bimatoprost and travoprost for first-line use based on the data that supported a first-line indication for Xalatan. FDA simply has no way of knowing, in the absence of data specific to the Allergan and Alcon products, whether those products are appropriate for use as first-line treatments.

FDA's decision to approve the Allergan sNDA, and its consideration of the Alcon sNDA, appears to reflect a class judgment that because one prostaglandin (latanoprost) has been shown to be safe for use as a first-line agent, all prostaglandins (or the related prostamides) are safe for such use. FDA historically has avoided inductive reasoning of this sort, however, recognizing that significantly different safety profiles can exist within a given therapeutic class of drugs. This issue was most recently addressed by an FDA panel at the Drug Information Association CDER Town Hall meeting on June 22, 2006. Dr. Robert Temple (Director, FDA Office of Medical Policy) stated explicitly that he could not think of a drug where class efficacy or safety had been the basis for approval.[12] Dr. John Jenkins (Director, FDA Office of New Drugs) added that safety and efficacy are not considered by the same standards, and that FDA would be extremely unlikely to extrapolate across a class for safety findings.

[12] A review of available public information appears to confirm this view that FDA has not used class efficacy or safety has the basis of approval. Throughout the history of class labeling, FDA has been vigilant when considering whether to expand class labeling to ensure that substantial data exist among *and across* the class, typically in the form of multiple studies involving thousands of patients and each drug in the class (*e.g.*, class labeling for hypertensives (1995), inhaled corticosteroids (1998), anti-TNF rheumatoid arthritis drugs (2001) and glitazones (1999)).

Important examples demonstrate the wisdom of FDA's caution.

a. In ophthalmology, the topical beta-blocker Optipranolol eye drops (metipranolol 0.6%) was withdrawn from the market place in 1990 due to major safety concerns following several cases of acute anterior uveitis and blepharoconjunctivitis. These safety concerns appeared to be associated only with Optipranolol, and did not arise with other topical beta blockers.

b. A similar cautionary tale comes from the class of "statin" medications. In 2001, Baycol (cerivastatin) was withdrawn from the market following reports of sometimes fatal rhabdomyolysis, a severe muscle adverse reaction from this cholesterol-lowering (lipid-lowering) product. While all statins have been associated with very rare reports of rhabdomyolysis, cases of fatal rhabdomyolysis in association with the use of Baycol were reported significantly more frequently than for other approved statins.

These examples illustrate the fact that the performance and safety of a given product cannot be assumed to be paralleled by other products within the same therapeutic class (Akingbehin 1991; Melles 1994). Thus, FDA generally requires specific efficacy and safety data for each individual agent before broadening the agent's use.

The science behind this approach is compelling and necessitates that FDA withdraw its approval of the Allergan sNDA and deny approval for the Alcon sNDA. Pfizer is aware of no evidence that would justify the presumption that all prostaglandins and the related prostamides are, as a class, equally safe for first-line use. As noted above, there are significant structural and functional differences among these three products. Thus, FDA's apparent decision to broaden the use of bimatoprost and travoprost, notwithstanding the absence of evidence establishing the safety of those products for such broadened use, seems inappropriate.

C. It is Arbitrary and Capricious to Treat Similarly Situated Parties Differently

Pfizer further urges FDA to withdraw its approval of the Allergan sNDA, and to deny approval of the Alcon sNDA, on grounds that it is arbitrary and capricious for the agency to grant the Allergan and Alcon first-line indications in the absence of data supporting such indications, when it previously required Pfizer to conduct extensive studies in order to obtain a first-line indication for Xalatan.

Courts have ruled that an agency must "treat similar cases in a similar manner unless it can provide a legitimate reason for failing to do so." *See Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27 (D.D.C. 1997), citing *Independent Petroleum Association of America v. Babbitt*, 92 F.3d 1248, 1258 (D.C. Cir. 1996). "If an agency treats similarly situated parties differently, its action is arbitrary and capricious and violation of the APA." See id., citing *Allergan Inc. v. Shalala*, 6 Food and Drug Rep. 389, 391, No. 94-1223 (D.D.C. Nov. 10, 1994).

Xalatan, Lumigan and Travatan were all initially approved by FDA for second-line treatment of high IOP. In supplements to the original NDAs, the sponsor of each drug has sought or is now seeking a first-line indication. In this sense, the three sponsors are similarly situated parties with respect to FDA's review process.

In order to gain a first-line indication for Xalatan, Pfizer submitted extensive and time-consuming additional studies in response to FDA requests. These additional submissions included:

- A 5-year long-term safety study including 344 patients;
- A 5-year, comprehensive post-marketing surveillance study involving 5000 patients;
- Morphological examinations of trabeculectomy specimens taken from patients treated with latanoprost for up to 41 months;
- A study of melanin in the trabecular meshwork of latanoprost patients; and
- Five years of post marketing experience during which time approximately 17 million patients were treated with latanoprost.

Pfizer is unaware of a similar complement of robust studies or safety data assembled by either Allergan or Alcon in support of a first-line indication for Lumigan or Travatan, respectively. For this reason, FDA should revoke the approval of Lumigan for a first-line indication and should withhold similar first-line approval for Travatan.

Environmental Impact

The petition requests that FDA review the applications for first-line indications for Lumigan and Travatan. Because the requested action would not increase the use of an active moiety, the petition is subject to a categorical exclusion from the requirement of an environmental impact assessment. *See* 21 C.F.R. §25.31(a).

Economic Impact

Information on the economic impact of this petition will be submitted if requested by the Commissioner.

Certification

Pfizer certifies, that, to the best knowledge and belief of Pfizer, this petition include all information and views on which the petition relies and that it includes representative data and information known to Pfizer which are unfavorable to the petition.

Respectfully submitted,

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