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UNITED STATES DISTRICT COURT

FOR THE CENTRAL DISTRICT OF CALIFORNIA

VALEANT PHARMACEUTICALS INTERNATIONAL, **Plaintiff,** **v.** **KATHLEEN SEBELIUS; JOSHUA M. SHARFSTEIN, M.D.,** **Defendants.** **and** **SPEAR PHARMACEUTICALS, INC.,** **Intervenor-Defendant.**	**CASE NO. SACV 08-0449-AG(AGRx)** **ORDER ON MOTIONS FOR SUMMARY JUDGMENT**

In this case, Plaintiff Valeant Pharmaceuticals, International ("Valeant") challenges a decision by the Food and Drug Administration ("FDA") to approve a generic drug. All three parties to this case have filed motions for summary judgment. After considering all papers and arguments submitted, the Court finds that the FDA's actions were not "arbitrary, capricious, an abuse of discretion or otherwise contrary to law" under the Administrative Procedures Act. Accordingly, the motions of Intervenor Spear Pharmaceuticals, Inc. ("Spear") and the Federal Defendants are GRANTED. For the same reasons, the motion of Plaintiff Valeant is DENIED.

BACKGROUND

The following facts are taken from the administrative record ("AR") in this case.

Valeant manufactures and markets Efudex cream, an FDA-approved "pioneer" or "brand-name" drug. Efudex is used to treat two skin conditions: (1) superficial basal cell carinoma ("sBCC"), a common form of skin cancer; and (2) actinic keratosis ("AK"), a condition involving skin lesions caused primarily by overexposure to the sun. (AR 658.) In June 1999, Spear began the process of seeking FDA approval to market a generic version of Efudex. (AR 938-39.) Spear intended to file an Abbreviated New Drug Application ("ANDA"), which is used for FDA approval of generic drugs. (AR 939.) The sponsor of an ANDA must establish, among other things, that the generic is "bio-equivalent" to the pioneer drug. *See* 21 U.S.C. § 355(2)(a)(iv).

At that time, and at all times relevant to this action, the FDA's Center for Drug Evaluation and Research (the "Center") was charged with reviewing ANDAs. The Office of Generic Drugs (the "Office"), a subdivision of the Center, was tasked with reviewing ANDAs like Spear's. The Office maintained a Division of Bioequivalence. When the Office reviewed data that was "outside the expertise of its staff" and needed to "reach a scientific and/or regulatory decision," it was required to "send the information to another part of [the FDA] for review." (Manual of Policies and Procedures, *Issuing and Tracking of Consults*, MaPP 5200.6 (May 9, 2001).) Because the generic version of Efudex was to treat skin conditions, the Office consulted the Division of Dermatology and Dental Drug Products (the "Division of Dermatology").

The Division of Dermatology has at all relevant times been headed by a dermatologist who holds the title of Director. Between 1994 and 2005, Dr. Jonathan Wilkin ("Wilkin") served as Director of the Division of Dermatology. (AR 1047.) He was succeeded by Dr. Susan Walker ("Walker"). In 1999, the Office of Generic Drugs first consulted the Division of Dermatology regarding the appropriate clinical study necessary to determine bioequivalence between Spear's proposed generic and Efudex. (AR 947.)

On November 9, 1999, the Division of Dermatology responded to the Office of Generic Drugs, stating that "[e]fficacy in the primary indication [AK] may be extrapolated if a secondary indication [sBCC] has similar pathology and is easier to treat." (AR 949.) The memorandum concluded that neither factor could be established. "Although both actinic keratosis and superficial basal cell carcinoma may arise in sun-damaged skin, their pathologies are not similar. Moreover, it is unlikely that superficial basal cell carcinoma is any easier to treat than actinic keratosis." (AR 949.) Wilkin sent and initialed the memorandum, which concluded that a study in AK alone was insufficient to establish bioequivalence. (AR 947.) Nevertheless, on December 10, 1999, the FDA informed Spear that it could conduct its clinical tests on AK patients only, concluding that "a study [involving sBCC] would be hard to execute" and "a second indication" would "not be necessary." (AR 945-46.) As Spear planned its clinical study on AK patients, the Office of Generic Drugs continued to consult the Division of Dermatology and Wilkin. (*See* AR 977-82.)

In December 2004, Spear submitted its ANDA to the FDA for review. (AR 1047.) That same month, Valeant filed a Citizen's Petition urging the FDA to require that any proposed Efudex generic be first tested on cancer patients, arguing that success of the drug in treating AK did not provide sufficient evidence that the drug delivered the requisite amount of active ingredient to cancerous skin cells. (AR 2.)

In response to the Citizen's Petition, the Office of Generic Drugs consulted the Division of Dermatology regarding the necessity of testing Spear's proposed drug on cancer patients. (AR 627.) On October 27, 2005, the Division of Dermatology sent another consult memorandum, recommending "not using solely AK (although the easier indication to study) for a bioequivalence evaluation." (AR 630.) The memorandum also recommended that "both AK and sBCC should be studied to yield independent confirmation of bioequivalence for these indications." (AR 630.) The memorandum was signed by Stanka Kukich, Acting Director of the Division of Dermatology. (AR 627.) In about November 2005, Wilkin left the FDA, while Spear's ANDA and Valeant's Citizen's Petition were still pending. (AR 1047.)

On June 26, 2006, the FDA held a teleconference to determine whether testing on cancer

patients would be required for Spear's clinical study. (AR 631-32.) Fifteen FDA officials conferred, including Susan Walker ("Walker"), Director of the Division of Dermatology, and Julie Beitz ("Beitz"), Acting Director of the Office of Drug Evaluation III. The Dermatology Division argued that cancer patients should be included in Spear's bioequivalence study, as AK and sBCC involve different types of tumors, and "[t]he consequences of any difference in delivery of the drug product would be more significant in sBCC and would impact the public health if it did not perform the same." (AR 631-32.) The Office of Generic Drugs then argued that cancer patients did not need to be included in the study, as the purpose of the bioequivalence study was merely to "demonstrate that the delivery to the site of action is the same for the test and reference products," and not to "demonstrate the underlying efficacy of the drug substance." (AR 632.) The Office added that the study conducted on AK patients demonstrated "that the products perform the same although the formulations are different" and provided evidence "that the drug is delivered to the level of the epidermis where AK occurs." (AR 632.) The Office concluded that "[t]he results in AK patients should provide confidence that the drug will also be delivered to the level of the epidermis where sBCC occurs." (AR 632.) In the end, the committee concluded that "sBCC should be the indication that should be studied in the bioequivalence study," and that "both indications need not be studied, as sBCC could be the sole indication for a bioequivalence study." (AR 632.)

In February 2007, the Office of Generic Drugs circulated a memorandum recommending the denial of Valeant's Citizen's Petition. (AR 636.) The Dermatology Division responded in a memorandum dated March 1, 2007, and reiterated that "the position of the Division of Dermatology and Dental Products" was "that both indications AK and sBCC should be evaluated in bioequivalence studies as proposed by the Petitioner." (AR 660.)

In March 2007, Spear retained Wilkin, former Director of the Dermatology Division, to act as its expert consultant. (AR 1047.) On March 14, 2007, Spear submitted a written opinion authored by Wilkin to the FDA. The submission asserted that bioequivalence testing for Spear's generic product did not need to include a clinical study for cancer patients.

The FDA turned to Beitz, Acting Director of the Office of Drug Evaluation III, for a

recommendation on Spear's ANDA and Valeant's Citizen's Petition. On December 3, 2007, Beitz drafted a memorandum recommending approval of Spear's ANDA and denial of Valeant's Citizen's Petition. (AR 727.) Beitz expressly cited Wilkin's letter in reaching her conclusion. (AR 727.)

On April 11, 2008, the FDA approved Spear's ANDA and denied Valeant's Citizen's Petition. On April 25, 2008, Valeant filed a complaint in this Court alleging violations of the Administrative Procedures Act.

On April 30, 2008, the FDA informed the Court that it had discovered a "potential conflict of interest . . . that could cause it to revisit the approval status of the ANDA." And on May 14, 2008, the Commissioner of the FDA concluded that "the FDA must reconsider" the approval of Spear's ANDA. (AR 1087.)

The FDA claims that it then attempted to determine whether Spear's ANDA would have been approved "if Dr. Wilkin had not made his March 14, 2007 submission." (AR 1107.) The matter was referred back to Beitz, and on May 29, 2008, Beitz wrote a memorandum concluding that she would have, in fact, recommended approval of Spear's ANDA even without the Wilkin submission. Beitz wrote:

> Removal of Dr. Wilkin's March 14, 2007 submission from consideration does not alter any of the conclusions that I reached in my December 3, 2007 memo regarding the adequacy of Spear's AK study to support approval of its product.

Beitz noted that three comments made in the Wilkin submission were particularly important: (1) a statement that "it is well-known and accepted that the greatest barrier to penetration through the skin is the stratum corneum"; (2) comments regarding the differences in the histopathology of the stratum corneum in AK versus sBCC; and (3) a comment that a bioequivalence study for AK was appropriate because the drug's labeling states that it is "recommended" for AK, but only "useful" for sBCC. (AR 1107-08.) Beitz noted that all three comments consisted of information

the FDA had considered even before the Wilkin submission. The information regarding the stratum corneum as the greatest barrier to skin penetration was clearly considered in a February 20, 2007 memo written by the Office of Generic Drugs. (AR 1107; *see also* OGD Mem. dated Feb. 20, 2007 memo at 9 ("As acknowledged by the petitioner, the stratum corneum is widely considered to be the predominant barrier to topical drug delivery.").) Wilkin's statements comparing the stratum corneum in AK and sBCC cases were supported by a document attached to Valeant's Citizen's Petition, submitted to the FDA long before the Wilkin submission. (AR 1108; *see also* Tab C to Valeant's Citizen's Petition.) Finally, Beitz noted that Wilkin's comment regarding the appropriateness of a bioequivalence study examining only AK patients "added only cumulative information to the record before the agency." (AR 1108; *see also* OGD memo dated Feb. 20, 2007 at 2-3; 13-15.)

On May 30, 2008, the other three reviewers – Drs. Woodcock, Throckmorton, and von Eschenbach – issued a "Decision on Reconsideration" reaffirming the approval of Spear's ANDA.

On June 2, 2008, the Court granted Valeant's motion for a temporary restraining order and compelled the Federal Defendants to suspend approval of Spear's ANDA. The Court also issued an order to show cause why a preliminary injunction should not issue. On June 18, 2008, the Court discharged the order to show cause and denied Valeant's request for a preliminary injunction.

Valeant now moves for summary judgment that the FDA's actions were improper under the Administrative Procedures Act. Spear and the Federal Defendants, on the other hand, move for summary judgment that the FDA's actions were proper under the Administrative Procedures Act and should be affirmed.

LEGAL STANDARD

Under the Administrative Procedures Act ("APA"), a reviewing court may set aside an agency action if it is "arbitrary, capricious, an abuse of discretion or otherwise contrary to law."

5 U.S.C. § 706(2)(A). But courts "do not rubberstamp agency actions," as doing so would be "tantamount to abdicating the judiciary's responsibility under the Administrative Procedures Act." *Nat'l Res. Defense Council v. Daley*, 209 F.3d 747, 755 (D.C. Cir. 2000). The Supreme Court had made clear that "[t]he essence of judicial review of administrative action is scrutiny" of the decision-making process. *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins.*, 463 U.S. 29, 43 (1983).

ANALYSIS

Valeant argues that the FDA's actions were "arbitrary, capricious, an abuse of discretion or otherwise contrary to law" under the Administrative Procedures Act. The appropriate remedy, Valeant asserts, is to revert to the FDA's consensus opinion reached before the taint in the review process. Both Spear and the Federal Defendants, on the other hand, argue that the FDA's approval of Spear's generic Efudex was proper. The Court agrees with Spear and the Federal Defendants.

Valeant first argues that the FDA improperly ignored the opinions of its dermatology experts. "Although the Court must defer to an agency's expertise, it must do so only to the extent that the agency utilizes, rather than ignores, the analysis of its experts." *Defenders of Wildlife v. Babbitt*, 958 F. Supp. 670, 685 (D.D.C. 1997); *Tummino v. Torti*, 603 F. Supp. 2d 519 (E.D.N.Y. 2009); *Center for Biological Diversity v. Lohn*, 296 F. Supp. 2d 1223, 1239-40 (W.D. Wash. 2003); *Latecoure Int'l v. U.S. Dep't of Navy*, 19 F.3d 1342 (11th Cir. 1994). Here, Valeant contends that "[t]he [r]ecord establishes that the FDA, as an agency, repeatedly sought the advice of its own experts, and then refused to defer to these experts." (Valeant Mot. 17:19-20.) Valeant also asserts that "during the brief and highly flawed reconsideration process," the FDA "did not even bother to seek (let alone follow) the advice of its own experts in the Dermatology Division." (Valeant Mot. 17:21-23.) The Court disagrees.

As this Court has previously found, the administrative record here "indicates that there was a scientific debate among the scientists at [the Division of Dermatology] and the Office of

Generic Drugs, as well as their supervisors and that the opinions upon which Valeant relies were considered." (June 18, 2008 Order ¶ 33.) But "it was ultimately determined by the experts in bioequivalence in the Office of Generic Drugs that an sBCC clinical study was not required." (June 18, 2008 Order ¶ 33.) Valeant has offered no evidence that the FDA actually ignored the opinions of its dermatology experts. The FDA simply did not defer to those opinions. As the Court noted in its June 18, 2008 Order, "deference is owed to the decisionmaker authorized to speak on behalf of the agency, not to each individual agency employee." (June 18, 2008 Order ¶ 34 (citing *Serono Labs. v. Shalala*, 158 F.3d 1313, 1321 (D.C. Cir. 1998)).) In this case, "the authorized decision maker in connection with Spear's original approval was the Office of Generic Drugs, not the dermatologists in the Office of New Drugs, and the authorized decision makers in connection with the reaffirmation of Spear's approval were Drs. Throckmorton, Woodcock, and von Eschenbach." (June 18, 2008 Order ¶ 34.) Valeant's first argument fails.

Valeant next argues that the FDA failed to remove the influence of the Wilkin submission from its decisionmaking process, but instead "engaged in an expedited and conclusory reconsideration." (Valeant Mot. 21:1.) Again, the Court disagrees. Contrary to Valeant's suggestion, Beitz's May 29, 2008 memorandum did not "purport[] to remove [Wilkin's] influence by claiming his opinions and reasoning were correct and claiming to have found support for them in the literature." (Valeant Mot. 21:3-5.) In her May 29, 2008 memorandum, Beitz examined each of Wilkin's key contentions and concluded that the information was available to the FDA before Wilkin's submission. Beitz thus concluded that even in the absence of Wilkin's submission, she and the FDA would have reached the same conclusion. Valeant's second argument fails.

After a thorough review of the administrative record, the Court is satisfied that the FDA's actions here were not "arbitrary, capricious, an abuse of discretion or otherwise contrary to law" under the Administrative Procedures Act. No genuine issues of material fact remain. Spear and the Federal Defendants are entitled to summary judgment, and their motions are GRANTED. The motion filed by Valeant is DENIED.

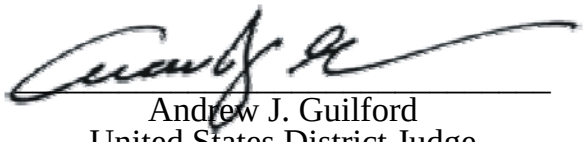
DISPOSITION

The motions for summary judgment filed by Spear and the Federal Defendants are GRANTED, and the FDA's approval of Spear's ANDA is affirmed. The motion for summary judgment filed by Valeant is DENIED.

Either Spear or the Federal Defendants shall file a brief, concise proposed judgment with the Court within 14 days of this Order.

IT IS SO ORDERED.

DATED: September 14, 2009



Andrew J. Guilford
United States District Judge