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UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

SOUTHERN DIVISION

VALEANT PHARMACEUTICALS INTERNATIONAL

Plaintiff

v.

KATHLEEN SEBELIUS, *in her official capacity as Secretary of the U.S. Department of Health and Human Services and* JOSHUA M. SHARFSTEIN, M.D., *in his official capacity as Commissioner of the Food and Drug Administration,*

Defendants.

and

SPEAR PHARMACEUTICALS, INC.

Intervenor Defendant.

Case No. SACV 08-0449 AG (AGRx)
Hon. Andrew J. Guilford

VALEANT PHARMACEUTICALS INTERNATIONAL'S NOTICE OF MOTION AND MOTION FOR SUMMARY JUDGMENT;

MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT;

RULE 56-1STATEMENT OF UNCONTRAVERTED FACTS AND CONCLUSIONS OF LAW; and

[PROPOSED] JUDGMENT

Hearing: July 20, 2009
Time: 10:00 a.m.
Dep't: 10D

Plaintiff Valeant Pharmaceuticals International ("Valeant") hereby gives notice that on July 20, 2009, at 10:00 a.m., or as soon thereafter as counsel may be heard, in Department D of the above-entitled Court, located at the United States Courthouse, 411 West Fourth Street, Santa Ana, California, 92701, Valeant will, and hereby does, move the Court for summary judgment against the U.S. Department of Health and Human Services ("HHS") and U.S. Food and Drug Administration ("FDA") (collectively, the "Federal Defendants") pursuant to Rule 56 of the Federal Rules of Civil Procedure.

Valeant moves for summary judgment on the following grounds:

Pursuant to the Administrative Procedures Act, the Court should hold unlawful, and set aside, each of the following actions as arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law: (i) the final approval of Defendant-Intervenor Spear Pharmaceutical's ("Spear's") generic version of Valeant's pioneer drug product, EFUDEX® (fluorouracil) 5% Cream ("Efudex Cream"); (ii) the re-affirmance of Spear's Abbreviated New Drug Application ("ANDA") No. 77-524; and (iii) the FDA's denial of Valeant's Citizen's Petition regarding the proper clinical bioequivalence testing that should be required to be performed prior to approval of any generic for Efudex Cream. These decisions were "arbitrary, capricious, an abuse of discretion or otherwise contrary to law" pursuant to 5 U.S.C. § 706(2) of the Administrative Procedure Act because the Federal Defendants (1) failed to defer to the relevant agency expertise; and (2) failed to remedy a significant conflict of interest that arose during, and tainted, the decision-making process.

Valeant not only requests that the Court set aside these decisions, but requests that the Court remand these issues to the Federal Defendants with instructions to implement the consensus decision, reached by the FDA on or about June 26, 2006, prior to the submission of the expert opinion that caused the taint.

This motion is based upon this Notice of Motion and Motion, the accompanying Memorandum of Points and Authorities, the Separate Statement of Uncontroverted Facts and Conclusions of Law, the Administrative Record on file, or as supplemented, in this action, and upon such other matters as may be presented to the Court at the time of hearing

This motion is made following the conference of counsel pursuant to Local Rule 7-3 which took place on April 30, 2009.

DATED: June 8, 2009

VALLE & ASSOCIATES

By: _____
Jeffrey B. Valle
Attorneys for Plaintiff
VALEANT PHARMACEUTICALS INTERNATIONAL

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INTRODUCTION

In this case, Valeant seeks to set aside the FDA's approval of Spear's ANDA ("Abbreviated New Drug Application"), which permits Spear to market a generic version of Valeant's Efudex® Skin Cream ("Efudex"). Valeant also seeks to set aside the FDA's related denial of Valeant's Citizen's Petition regarding the proper clinical bioequivalence required for approval of any generic for Efudex.

Spear asked the FDA to approve its generic version of Efudex for treatment of two skin disorders -- actinic keratosis ("AK"), a form of sun-damaged skin, and superficial basal cell carcinoma ("sBCC"), a form of skin cancer. Although Spear's generic would be used to treat skin cancer, Spear sought approval to conduct a limited clinical test only on AK patients, not cancer patients.

Since the issue presented to the FDA involved a cream for the treatment of two *skin* disorders, the FDA consulted with the relevant experts within the agency, the Dermatology Division. The Dermatology Division unanimously and repeatedly advised that Spear's clinical tests must test for bioequivalence on skin cancer patients, not only AK patients. From 1999 through 2007, the Dermatology Division expressed this view in (at least) four separate Consult Memorandums. And in June 2006, in an all-hands conference with fifteen representatives from all relevant groups within the FDA, the FDA reached a consensus conclusion that Spear should be required to test its generic on skin cancer patients.

In an effort to change the FDA's view, Spear retained Dr. Jonathan Wilkin as its expert consultant. Dr. Wilkin had been the Director of the FDA's Dermatology Division from 1994 until his departure in or about November 2005. He had been directly involved in reviewing Spear's ANDA, including personally signing-off on Consult 129, which advised that Spear should be required to test its generic on skin cancer patients. He also supervised the Division that repeatedly gave this advice.

As Spear's paid consultant, Dr. Wilkin took the exact opposite position he had taken while at the FDA. As a hired gun, his opinion was that Spear could get away with testing its generic only on AK patients. On March 14, 2007, Dr. Wilkin submitted his new opinion to Spear, who then promptly transmitted it to the FDA.

Dr. Wilkin's submission had the desired effect of turning around the FDA. Dr. Julie Beitz, a key decision-maker here, reviewed Dr. Wilkin's submission and **reversed her opinion** that testing on skin cancer patients should be required to correspond to Dr. Wilkin's new position (that it should not be required). Dr. Beitz drafted a memorandum, dated December 3, 2007, citing Dr. Wilkin's submission and adopting his new reasoning *in toto*. The Beitz memorandum proved decisive. On April 11, 2008, Spear's ANDA (permitting it to test its generic only on AK patients) was granted and Valeant's Citizen Petition was denied.

Once Valeant had filed this suit, the FDA was forced to acknowledge that Dr. Wilkin's submission should not have been considered because he "had been directly involved in considering the same issue while employed at the FDA" and determined that the FDA needed to reconsider its approval of the ANDA.

The FDA's reconsideration, however, was a sham. Rather than seek out an independent voice, it referred the matter back to Dr. Beitz, the key decision-maker who had relied on Dr. Wilkin's paid for opinion in recommending that the FDA approve Spear's ANDA. Although she was supposed to reconsider her recommendation without relying on Dr. Wilkin, Dr. Beitz did not do so. She arrived at the same conclusion (that Spear's ANDA should be approved), because, according to her, there was support for his reasoning in medical literature. Dr. Throckmorton adopted the reasoning from Dr. Beitz' December 3, 2007 tainted memorandum, and Drs. Woodcock and Von Eschenbach simply rubber-stamped the reconsideration. The entire reconsideration process took only two weeks.

In its result-oriented approach, the FDA shut out the Dermatology Division during the reconsideration process, even though the dermatologists had the relevant

expertise, had previously unanimously advised that Spears generic be tested on skin cancer patients, and had not been tainted by Dr. Wilkin's improper submission.

Notably, Valeant is not asking the Court to substitute its judgment for the scientific judgments of the FDA; rather, Valeant is asking the Court to scrutinize the flawed procedures used by the FDA – procedures which ultimately circumvented the scientists within the FDA who held the relevant expertise. While in the ordinary case, an FDA determination is entitled to deference by the courts, this is not an ordinary case. The FDA's approval of Spear's ANDA and denial of Valeant's Citizen Petition must be vacated for the following two independent reasons.

First, the FDA repeatedly ignored the unanimous view of its own experts. It is well-established that where an administrative agency ignores the analysis of its own experts, its decision is entitled to no deference at all. Here, the FDA's experts in the Dermatology Division unanimously and repeatedly advised that Spear should be required to test its generic on skin cancer patients. In light of the FDA's complete and willful disregard of its own experts, the Court should find that the FDA acted irrationally, capriciously and abused its discretion.

Second, the FDA's entire approval process was tainted by Dr. Wilkin's improper submission. Dr. Wilkin violated the federal "2-year" ban (18 U.S.C. § 207 (a)(2)), which prohibits former agency officials from seeking to influence the federal government on a particular matter during that period. In any event, the FDA admits, as it must, that it should not have considered Dr. Wilkin's submission because he was personally involved in the Spear matter while at the FDA. The process used to carry out its own purported resolution of this conflict was clearly irrational, and constituted a reversible abuse of discretion.

The issue presented by this case is not trivial. It involves an important matter of public health and safety. The FDA's own dermatology experts recognize that Spear should not be permitted to market its generic as effective as Efudex in treating skin cancer without having any evidence from clinical trials that it is. The opinion

of the FDA experts, who unlike Dr. Wilkin were supposed to protect the public's interest as opposed to advocate on behalf of a client for money, is correct. The FDA's ruling approving Spear's ANDA and denying Valeant's Citizen Petition must be vacated.

STATEMENT OF FACTS

A. Valeant's Efudex Cream Is Unique Because It Is Approved To Treat Both Skin Cancer And Non-Cancerous Skin Lesions

Valeant manufactures and markets Efudex Cream, an FDA-approved "pioneer" or "brand-name" drug. Efudex Cream is used to treat sBCC (superficial basal cell carcinoma), a common form of skin cancer. (AR at 658.) Ineffectively treated, sBCC can lead to further growth into other parts of the skin, and in some instances, metastasize to nearby parts of the body. (AR at 660.) Efudex Cream is also used to topically treat AK (actinic keratosis), which are skin lesions caused primarily by overexposure to the sun. (AR at 658.)

Efudex Cream was first approved by the FDA over 30 years ago for the treatment of sBCC. To this day, Efudex Cream (5%) remains the only topical fluorouracil cream on the market that has a history of safe and effective treatment of sBCC. Notably, Valeant has licensed the distribution of a generic version of Efudex so, even without Spear's unproven product, there is a generic available to the public in the marketplace.

The FDA has approved other fluorouracil cream and solution products, in 0.5%, 1%, and 2% strengths, for use in treating AK; however, none of these products has been shown to be safe and effective in treating sBCC. (AR at 658, n.1.)

B. Spear Approached The FDA With Plans To Market A Generic Version Of Efudex Cream

In or about June of 1999, Spear began the process of seeking FDA approval to market a generic version of Valeant's Efudex Cream. (AR at 938-39.) The Record indicates that Spear was preparing to file an Abbreviated New Drug Appli-

cation ("ANDA"), which is used for FDA-approval of generic drugs. (AR 993.) The sponsor of an ANDA, must establish, *inter alia*, that its generic drug is "bioequivalent" to the pioneer drug. *See,e.g.*, 21 U.S.C. 355(2)(a)(iv).[1]

At the time, and throughout all periods relevant to this case, the FDA's Center for Drug Evaluation and Research was directly charged with reviewing ANDAs. The Center is subdivided into "Offices." The Office of Generic Drugs is tasked with reviewing ANDAs, including Spear's ANDA for a generic version of Efudex. The Office of Generic Drugs did not employ teams of physicians or clinical experts in particular therapeutic areas (e.g., dermatology). Rather, it maintained a Division of Bioequivalence.

When the Office of Generic Drugs received data for review that is "outside the expertise of its staff" and needs to "reach a scientific and/or regulatory decision," it is 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) ("To reach a scientific and/or regulatory **d**ecision, OGD *must* send the information to another part of CDER for review."). This is done through a Consult request. "Common examples of issues that require a consult request include safety evaluations of inactive ingredients, some labeling reviews, some bioequivalence protocol reviews, and statistical reviews of bioequivalence studies.") (*Id.*) Often the "Consults" are directed to specialized divisions within the Office of New Drugs.

In this case, because the drug treats two skin disorders, the Division of Dermatology and Dental Drug Products (the "Division of Dermatology") possessed the

[1] Spear had submitted the details of its proposed bioequivalence study to the FDA for review and comment. (AR 993.) Although the FDA could provide comments and feedback, it cannot be bound by any comments or feedback provided to Spear because of its crucial gate-keeping function. Among other things, the relevant science may evolve, requiring revisions in study protocol.

relevant expertise. That is why the Office of Generic Drugs repeatedly sought Consults from the Division of Dermatology in this matter.

1. In 1999, The FDA's Dermatology Experts Recommended Testing on Cancer Patients

The Division of Dermatology is generally responsible for providing advice on dermatological issues to officials throughout the FDA, and for approving new dermatological drugs. (Federal Defendant's Answer to FAC at ¶6 admitting same). At all relevant times, it has been headed by a medical doctor – a dermatologist – who holds the title of Director. From 1994 until about November 2005, Dr. Jonathan Wilkin was the Director of the Division of Dermatology. (AR at 1047.) Dr. Susan Walker succeeded Dr. Wilkin as Division Director. (AR at 631.)

The Division of Dermatology employs a team of physicians with clinical dermatology and scientific expertise in, among other things, dermapathology, skin anatomy, and identifying the obstacles to absorption posed by various layers of skin.

In 1999, the Office of Generic Drugs first consulted with the Division of Dermatology about the appropriate clinical study necessary to determine bioequivalence between Spear's proposed generic product and Efudex. (AR at 944.) Dr. Wilkin, the Director of Dermatology, was copied on the email request. (*Id.*)

The Division of Dermatology concluded, and never wavered from its conclusion, that Spear was required to test its generic drug for sBCC, not simply AK. Thus, on November 9, 1999, the Division of Dermatology responded to the Office of Generic Drugs 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 at 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 basil cell carcinoma is any easier to treat that actinic keratosis." (AR at 949) (emphasis added).

The Division of Dermatology therefore concluded that a study in AK alone was insufficient. This memorandum was sent through, initialed, and adopted by, Dr. Wilkin. (AR at 947.)

But the Office of Generic Drugs ignored the FDA's own dermatology experts. Despite the experts' opinion, including the Division Director, Dr. Wilkin, the Office of Generic Drugs concluded that "a study [involving sBCC] would be hard to execute" and "a second indication" "would not be necessary." (AR at 945-46.) Thus, on December 10, 1999, the FDA informed Spear that it could conduct its clinical tests on AK patients only.

2. The FDA Continued To Consult the Division of Dermatology, And Dr. Wilkin, Regarding Spear's Proposed Clinical Study

Although it ignored its experts' conclusion about the need for a study on cancer patients, the Office of Generic Drugs nonetheless recognized that it needed to consult with the Division of Dermatology as questions arose concerning Spear's proposed clinical study. Dr. Wilkin, as Director, continued to be involved. (AR at 977-82.) (Dermatology Division Consult No. 149 regarding the need for a placebo arm in Spear's study, initialed and dated by Dr. Wilkin).[2]

C. Spear Submitted Its ANDA and Valeant Filed Its Citizen Petition

In December of 2004, Spear submitted its ANDA to the FDA for review. (AR at 1047.) Also in December 2004, Valeant filed a Citizen's Petition urging the FDA to require that any proposed Efudex generic should first be tested on cancer

[2] In 2003, the Administrative Record reflects that the Office of Generic Drugs sought yet another consult from the Division of Dermatology on the Spear matter. The Consult is identified in the record but the Consult itself had not been included in the Record. We therefore do not know the specific involvement of Dr. Wilkin in this Consult, which is one of the reasons Valeant has sought discovery to supplement or complete the Administrative Record. In any event, Dr. Wilkin was the head of the Division of Dermatology at the time of this Consult. At a minimum, therefore, the Consult occurred under his supervision.

patients, as success of the drug in treating sun-damaged skin does not provide evidence that the cream delivers the requisite amount of active ingredient to cancerous skin cells. (AR at 2.)

D. In 2005, FDA's Dermatology Experts Again Recommended Testing Cancer Patients

In responding to Valeant's Citizen Petition, the Office of Generic Drugs again asked the Division of Dermatology for a Consult on the necessity of testing Spear's proposed generic drug on cancer patients. The Office of Generic Drugs recognized that input from the Division of Dermatology was necessary to evaluating the issues raised in the Citizen Petition:

> [W]e believe that **input from your division will be needed** in order to finalize a response to the petition.

(AR at 627) (emphasis added).

The Division of Dermatology wrote the Consult Memorandum, dated October 27, 2005. (AR at 627-630.) The Acting Director for the Division of Dermatology, through which it was sent, signed and dated the Memorandum, indicating full approval. (*Id.*) Dr. Julie Beitz, an Office Director within the FDA, was copied on the Memorandum. The Memorandum concluded that:

> **DDDP recommends not using solely AK (although the easier indication to study)** for a bioequivalence evaluation. . . **DDDP recommends that both AK and sBCC should be studied** to yield independent confirmation of bioequivalence for these indications . . .

(AR at 630) (emphasis added).

E. In Late 2005, Dr. Wilkin Leaves The FDA

After serving as the head of the Dermatology Division since 1994, Dr. Wilkin left the FDA in or about November 2005. (AR at 1047.) The ANDA and Citizen Petition were both pending at the time Dr. Wilkin left the FDA.

F. **In 2006, The FDA Reached A Consensus Conclusion That Testing On Cancer Patients Was Necessary**

On June 26, 2006, the FDA held an all-hands meeting to determine whether testing on cancer patients would be required for the clinical study. (AR at 631-32.) The Office of Generic Drugs, the Division of Dermatology, the Division of Bioequivalence, the Office of Drug Evaluation III, and the Office of Regulatory Policy were all represented. (*Id.*) Many high-level officials attended, including, among others:

- **For The Office of Generic Drugs**:
  - The Director and the Deputy Director
  - The Director of Science
  - Associate Director of Medical Affairs (Dr. Dena Hixon) -- the Medical Review Officer Tasked With Reviewing Spear's ANDA;
- **For The Division of Bioequivalence** (in the Office of Generic Drugs):
  - The Director and the Deputy Director
- **For The Division of Dermatology:**
  - The Director (Dr. Susan Walker)
  - The Lead Medical Officer (Dr. Markam Luke)
- **For The Office of Regulatory Policy:**
  - Supervisory Regulatory Counsel and Regulatory Counsel
- **For the Office of Drug Evaluation III:**
  - Acting Director (Dr. Julie Beitz)

At the meeting, these fifteen FDA officials conferred. The Dermatology Division made the case that cancer patients should be included in any study seeking to establish bioequivalence to Efudex Cream:

- AK is a benign tumor, sBCC is a malignant tumor.
- The site of action in the epidermis differs for each type of tumor.
- A malignant tumor is more vascular and will facilitate transport of any drug substance.
- The biology of AK vs. sBCC is different.

- There are formulation differences in the proposed product which may affect the performance of the product.
- The 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 at 631-32.)

After the Office of Generic Drugs made its presentation, the group reached the consensus conclusion that testing on cancer patients was necessary. (AR at 632.) The minutes state unequivocally:

> **It was concluded [] that sBCC should be the indication that should be studied in the bioequivalence study . . . .**

(AR at 632) (emphasis added).

The conclusion was reached not by low-level employees, with minimal experience; but rather by the *Directors* of the Office of Generic Drugs, the Division of Bioequivalence and the Division of Dermatology (and its Lead Medical Officer).

G. In 2007, The FDA's Dermatology Experts Again Re-Affirmed That Testing On Cancer Patients Was Necessary

Although the Dermatology Division again had recommended that testing be done on cancer patients, in February 2007, the Office of Generic Drugs circulated a Memorandum recommending the *denial* of Valeant's Citizen Petition. (AR at 636.)

The Dermatology Division promptly responded in a Memorandum dated March 1, 2007. The Memorandum was sent through Dr. Beitz, among others, which indicates concurrence. The Memorandum reiterated that "the position of the Division of Dermatology and Dental Products" is "that both indications AK and sBCC should be evaluated in bioequivalence studies as proposed by the Petitioner." (AR at 660.) The Memorandum included the following observations:

- The Office of Generic Drugs "approaches topical drugs and their action as if the drugs were applied to a layered organ, i.e. skin. Unfortunately, such a model is an overly reductionist approach to the skin and may not accu-

rately reflect the microanatomy of the human body's largest organ, i.e. skin."

- This "reductionist approach to skin anatomy appears to have been applied to the examination of Spear's ANDA."
- "Actinic keratoses are not the same disease as superficial basal cell carcinoma. The two diseases have different behaviors and different outcomes."
- **"We recommend that the Office of Generic Drugs reconsider the 'one study fits both' approach. This approach should not be used when one of the indications in question is cancer and the other is not."**

(AR at 657-61.) (emphasis added).

H. Spear Retained Dr. Wilkin As An Expert Consultant And Submitted His *New Paid For* Opinion, On Behalf of Spear, That Testing On Cancer Patients Was Not Necessary

In or about March 2007, Spear retained Dr. Wilkin, the former Director of the Dermatology Division to act as its expert consultant. (AR at 1047.) As described above, Dr. Wilkin had been directly involved in the Spear matter at the FDA since its inception. While at the FDA, Dr. Wilkin had taken the position that Spear should be required to conduct its clinical studies on cancer patients, not just AK patients. *See e.g.* "Consult 129" (Dr. Wilkins's official recommendation that Spear's clinical study should include testing on cancer patients.). But, as Spear's paid expert consultant, he took the exact opposite position.

On March 14, 2007, Spear delivered Dr. Wilkin's written opinion to the FDA. (AR at 1047.) In this submission, Dr. Wilkin suddenly asserted that the bioequivalence testing for Spear's generic product need not include a clinical study of cancer patients. Dr. Wilkin does not cite any academic authority for his new opinion. Nor does he provide any explanation for changing his opinion. He instead relied on the

authority of his own reputation in the industry (and in the FDA).[3] As Spear touted in its transmittal letter: "As you are aware . . . Dr. Wilkin directed the [Division of Dermatology] from 1994 to 2005. He is therefore uniquely qualified to offer pivotal judgment on this longstanding issue."

I. After Dr. Wilkin's Submission, Dr. Beitz, A Division Director And Central Figure In Deciding Spear's ANDA And Valeant's Citizen Petition, Changed Her Opinion

Following Dr. Wilkin's submission, the FDA turned to Dr. Beitz, the acting Director of the Office of Drug Evaluation III, for her recommendation on Spear's ANDA and Valeant's Citizen Petition.

At all times prior to Dr. Wilkin's submission, Dr. Beitz had been part of the Consensus Conclusion within the FDA that Spear should be required to conduct its tests on cancer patients, not just AK patients. She participated in the FDA's all-hands conference in 2006 that reached this conclusion, and concurred in the Division of Dermatology Consult Memorandum, dated March 1, 2007, urging the Office of Generic Drugs to require testing on cancer patients.

But following Dr. Wilkin's submission, she suddenly changed her position. On December 3, 2007, Dr. Beitz drafted a memorandum recommending the *approval* of Spear's ANDA and the denial of Valeant's Citizen Petition based on her newly-formed view that bioequivalence could be established using a clinical study only AK patients and without testing cancer patients. (AR at 727).

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[3] Interestingly, Dr. Wilkin attached his Curriculum Vitae that highlighted, among other things, his prior FDA experience but omitted any mention of his then-current consulting business. He also submitted his opinion to Spear who then promptly transmitted it to the FDA, which may well suggest a conscious attempt to avoid the appearance of a direct submission to the FDA. Surely Dr. Wilkin was well aware that he had been directly involved in the Spear matter while at the FDA (signing off on Consults 129 and 149), that the matter was pending when he left less than two years earlier, and that he was the head of the division that repeatedly consulted with the Office of Generic Drugs on the matter.

Dr. Beitz's memorandum, which expressly cited Dr. Wilkin's submission, adopted the reasoning of Dr. Wilkin *in toto*. Inexplicably, Dr. Beitz did not copy anyone in the Dermatology Division (which held the contrary view).

The importance of Dr. Beitz's memorandum, and the influence of Dr. Wilkin on that memorandum, is great. Dr. Beitz's memorandum is the last internal document entered in the Administrative Record by the FDA prior to its approval of Spear's ANDA and denial of Valeant's Citizen Petition. As later admitted by Dr. Throckmorton, the Deputy Director for the Center of Drug Research: "Dr. Beitz memo served as a basis for the agency's April 11, 2008 response to the Valeant Citizen petition and its approval on the same date of the Spear ANDA." (AR at 1095).

On April 11, 2008, the FDA approved Spear's ANDA and denied Valeant's Citizen Petition. On or about April 25, 2008, Valeant filed a complaint alleging violations of the Administrative Procedure Act.

J. <u>After Valeant Filed Suit, The FDA Conceded That The Wilkin Submission Should Not Have Been Considered</u>

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."

On May 14, 2008, the Commissioner of the FDA concluded that "the FDA **must** reconsider the approval of [Spear's ANDA]." (AR at 1087.) (emphasis added). On the same day, the FDA sought an additional 14 day stay of the temporary restraining order this Court had issued and asked the Court to refer the matter back to the FDA for reconsideration under 21 C.F.R. § 10.33(h).

The FDA later disclosed that:

> [I]n the course of compiling the administrative record for the April 11, 2008 approval of Spear's ANDA, agency staff discovered that . . . **Dr. Wilkin had been directly involved in considering the same issue while employed by the FDA[.]**

(AR at 1095.) (emphasis added). The FDA concluded that: "**[b]ecause of Dr. Wilkin's prior involvement in this matter, it is not appropriate to consider his submission on behalf of Spear.**" (*Id.*) (emphasis added).

K. The FDA Failed To Remedy The Taint Created by Dr Wilkin's 2007 Submission

In a purported attempt to remove the taint from its original decision approving Spear's ANDA, the FDA claims that it set out to determine whether Spear's ANDA would have been approved "if Dr. Wilkin had not made his March 14, 2007 submission." (AR at 1107) (J. Beitz). The FDA did not seek an independent assessment of its prior approval decision either from its own dermatology experts at Division of Dermatology or from anyone else.

Incredibly, the FDA referred the matter back to Dr. Beitz – the key decision-maker who had relied upon Dr. Wilkin in her decisive December 3, 2007 memorandum. (AR at 1106).

While Dr. Beitz wrote a new memorandum dated May 29, 2008, she again relied on Dr. Wilkin's improper submission. (AR at 1106-09.) Essentially, she claimed that Dr. Wilkin's reasoning was right, that she still agrees with it, and that she can find support for it in academic literature, so he did not improperly influence the decision-making process. (*Id.*) What she did not do (and logically could not do, given her exposure to his submission) was what she was asked to do – determine if she would have reached the same result if he had not made his submission.

The Administrative Record further indicates that, following Dr. Beitz' May 29, 2008 Memorandum, the three other reviewers, Drs. Throckmorton, Woodcock and von Eschenbach, completed the reconsideration by *the next day*. The "Decision on Reconsideration" is dated May 30, 2008. (AR at 1088.)

Dr. Throckmorton, in his support for the Approval, acknowledged that Dr. Wilkin's submission should not be considered. (AR at 1091) (Wilkin opinion must be "omitted from consideration" on Reconsideration.) But he nonetheless relied

upon Dr. Beitz's December 3, 2007 memorandum, which was tainted by Dr. Wilkin's improper submission, citing it with approval at least five times. (AR at 1096-99.) In fact, he states that December 3, 2007 memorandum "elegantly summarizes the issues raised here and summarizes the science." (AR at 1096.) Dr Throckmorton also includes, as Attachment 2, Dr. Beitz's May 2008 memorandum. (AR at 1105-06.)

On May 30, 2008, Dr. von Eschenbach, the Commissioner of the FDA, stated that his endorsement of the re-affirmation of the approval of Spear's ANDA was "based on Dr. Woodcock's recommendation[.]" He further acknowledged that "Dr. Woodcock's recommendation was based on her review and assessment of a memorandum prepared by Douglas C. Throckmorton, M.D." (AR at 1088.)

The reconsideration process took a total of two weeks. Each of the four decision-makers (Drs. von Eschenbach, Woodcock, Throckmorton and Beitz) re-affirmed the approval of Spear's ANDA by either relying upon Dr. Wilkin's submission (which the FDA itself had determined "should not be considered") or FDA opinions derived from Dr. Wilkin's submission.

Incredibly, this time, there was no attempt to consult at all with the Dermatology Division – the recognized experts on the issue, who had consistently maintained that cancer patients must be tested, and who had not been exposed to Dr. Wilkin's improper submission.

LEGAL STANDARD

Under the APA, a reviewing Court is empowered to 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). While the standard of review is deferential, courts "do not rubberstamp agency actions. That 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 has 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).

As explained below, the decision-making process employed by the FDA constituted an abuse of discretion, both by failing to utilize agency expertise without any rational explanation and by failing to remedy an admitted taint consistent with its own protocol. The resulting decisions, therefore, are not the result of reasoned decision-making and, pursuant to the APA, should be set aside.

LEGAL ARGUMENT

I. THE FDA IMPROPERLY IGNORED ITS OWN DERMATOLOGY EXPERTS

"Although the Court must defer to an agency's expertise, it must do so [under the APA] 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) (under the APA, the FDA improperly denied Citizen Petition where it ignored the recommendations of agency experts); *Center for Biological Diversity v. Lohn*, 296 F. Supp. 2d 1223, 1239-40 (W.D. Wash. 2003) (agency erred when it "ignored its experts' conclusions"); *Latecoure Int'l v. U.S. Dep't of Navy*, 19 F.3d 1342, 1365 (11th Cir. 1994) (court overturned award of contract where Secretary of the Navy ignored the experts "charged with assisting in the decision").

A. The Relevant Expertise Is In The Dermatology Division

The relevant expertise on the proper clinical study to establish bioequivalence for Efudex, a cream approved for treating two *skin* disorders, is located within the Division of Dermatology. The conduct of the FDA demonstrates this fact. The Office of Generic Drugs (which did not employ teams of physicians or clinical experts in particular therapeutic areas) repeatedly sought Consults from the Dermatology Division, recognizing the "need" for their expertise.

Spear's conduct also demonstrates this fact. When Spear sought to influence the FDA, it retained the former head of the *Dermatology Division*, Dr. Wilkin, claiming that, as a result of that very expertise, he was "uniquely qualified to offer pivotal judgment on this long-standing issue." (AR at 1047.) And when the FDA overruled the unanimous view of its own Dermatology Division, it did so by relying on the outside opinion of a *dermatologist* – Dr. Wilkin. And even when it engaged in their misguided reconsideration process, it cited with approval, and relied on the reasoning of, the opinions of an "outside" *dermatologist* – Dr. Wilkin again.

B. The FDA Disregarded The Unanimous Opinion Of Its Own Dermatology Experts

It is undisputed that the FDA improperly ignored the unanimous recommendations of its own dermatology experts. From 1999 to 2007, doctors in the Dermatology Division who recommended testing on cancer patients included, *without limitation*: (1) Jonathan Wilkin, (2) Hon-Sum Ko, (3) Susan Walker, (4) Robert DeLap (AR at 947), (5) Markham Luke (AR 633), (6) Stanka Kukich (AR at 627), and (7) Patricia Brown (AR at 657). Some, such as Drs. Luke and Walker, did so repeatedly. Drs. Luke and Walker did so as Dermatology Team Leaders. Drs. Wilkin and Walker made these recommendations as Division Directors.

The Record establishes that the FDA, as an agency, repeatedly sought the advice of its own experts, and then refused to defer to these experts.

Moreover, 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. This failure is particularly troubling since the FDA's dermatologists had previously issued consistent and unanimous opinions directly contrary to the conclusion the FDA reached on reconsideration. But rather than test its conclusion with its own experts, the FDA instead relied on the reasoning of Spear's expert dermatologist (Dr. Wilkin) and sought to reconstruct his reasoning and conclusions from the literature.

Having wholly failed to defer to its own experts – who provided a unanimous and monolithic conclusion for literally seven years on this matter -- the Court must conclude as a matter of law that the FDA's decision was not the result of reasoned decision making and must be set aside. *Defenders of Wildlife*, 958 F. Supp. at 685; *Earth Island*, 494 F.3d at 766; *Tummino*, 603 F.Supp.2d at 519; *Center for Biological Diversity v. Lohn*, 296 F. Supp. 2d at 1239-40; *Latecoere*, 19 F.3d at 1365. The appropriate remedy for this abuse of discretion is addressed in Section III below.

II. DR. WILIKIN'S CONFLICT OF INTEREST TAINTED THE DECISION MAKING PROCESS

A. Although Congress Prohibits The FDA From Considering the Opinions of Recently Departed FDA Officials, The FDA Repeatedly Relied On The Wilkin Opinion

18 U.S.C. § 207(a)(2) prohibits a former employee of a government agency such as the FDA, for a period of two years after leaving the government, from knowingly making a communication or appearance, with intent to influence, before the government on behalf of another person, in connection with "a particular matter" involving specific parties, which the individual knew or should have known "was actually pending under his or her official responsibility" during the individual's last year with the government. *See also* 5 C.F.R. § 2637.202 (promulgated Feb. 1, 1980).

Valeant's Citizen Petition and Spear's ANDA were both pending when Dr. Wilkin left the FDA in or about November of 2005. As used in Section 207(a)(2), "actually pending" means "that the matter was in fact referred to or under consideration by persons within the employee's area of responsibility, not that it merely could have been." 5 C.F.R. § 2637.202(c). *See also* 68 Fed. Reg. 7844, 7879 (Feb. 18, 2003) ("A matter remains pending even when it is not under 'active' consideration.").

All "particular matters under consideration in an agency are under the 'official responsibility' of the agency head, and each is under that of any intermediate super-

visor having responsibility for an employee who actually participates in the matter within the scope of his or her duties." 5 C.F.R. § 2637.202(b)(2). Because Spear's ANDA and Valeant's Citizen Petition both required consult response memorandums from Dr. Wilkin's Division of Dermatology—one of which the Division was working on at the time of his departure from the FDA, these matters were pending under Dr. Wilkin's "official responsibility."

Indeed, Spear's ANDA and issues concerning the ANDA had been under consideration at the FDA from approximately 1999. Valeant's Citizen Petition was pending before the FDA between December 21, 2004 and April 11, 2008. From the beginning, Dr. Wilkin's Dermatology Division was significantly involved in the FDA's deliberations. Several Division employees wrote consult response memorandums, and Dr. Wilkin himself circulated emails about the Spear ANDA matter and personally approved multiple memoranda .

It is also undisputed that Dr. Wilkin's submission as a "paid for" consultant was presented to the FDA less than two years after his departure from the FDA. While Dr. Wilkin did not personally transmit his opinion to the FDA, he submitted it to Spear who immediately did so. It would obviously elevate form over substance, and neuter conflict of interest rule itself, if this tactic could immunize the improper influence of a former agency official.

Dr. Wilkin thus violated 18 U.S.C. § 207(a)(2) by communicating to the FDA in March 2007 that it should not require testing in sBCC patients in connection with a matter that he, personally, and the Division he supervised, were directly involved in and was still pending during his last year at the FDA: the agency's consideration of Spear's ANDA. His substantial involvement in the Spear matter probably triggers the lifetime ban as well. 18 U.S.C. § 207 (a) (1). But it is not necessary to reach this issue since it is undisputed that Dr. Wilkin's submission was made less than two years from his departure from the FDA.

As the Court explained in *United States v. Dorfman*, 542 F. Supp. 402, 410 (N.D. Ill. 1982), citing the Legislative History of Section 207:

> 18 U.S.C. § 207, like other conflict of interest statutes, seeks to avoid even the appearance of a public office being used for personal or private gain. In striving for public confidence in the integrity of government, it is imperative to remember that what appears to be true is often as important as what is true. Thus government in its dealings must make every effort to avoid even the appearance of a conflict of interest…

The FDA cannot argue that Dr. Wilkin's submission was an appropriate factor for the FDA to consider in reaching its conclusion. That is because the FDA itself concluded otherwise, and informed this Court otherwise. The FDA recognized that : (1) Dr. Wilkin "*had been directly involved in considering the same issue while employed by the FDA.*" (AR at 1095) (2) Dr. Wilkin's submission should not have been considered by the FDA (Id.); and (3) the FDA was therefore compelled to reconsider Spear's ANDA to make a determination without the influence of Dr. Wilkin. (*Id.*).[4]

Having acknowledged that it was obligated not to consider Dr. Wilkin's submission, the FDA's decision must be vacated if it did not in fact remove Dr. Wilkin's influence from its decision-making. As explained above, the FDA's reconsideration process wholly failed to remedy the taint of Dr. Wilkin's improper influence. The

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[4] The FDA has argued that its subsequent internal investigation concluded that Dr. Wilkin has not committed a criminal violation of section 207. However, the issue is not whether Dr. Wilkin committed a crime for which he should be prosecuted, but whether the FDA, in avoiding even the appearance of impropriety, must cleanse its decision-making from his influence. The FDA itself recognized that it was obligated to do so. Moreover, the subsequent investigation only analyzed whether Dr. Wilkin violated the lifetime ban (section 207(a) (1)) or the one-year ban (section 207 (a) (3)). *Inexplicably, the investigation did not analyze whether Dr. Wilkin violated the two-year ban (section 207(a) (2) – the section that most clearly applies to Dr. Wilkin's conduct here. See* Exhibits to Decl. of M. Bhatt in support of Spear's Motion.

FDA engaged in an expedited and conclusory reconsideration, spearheaded by Dr. Beitz, the person who had written the key tainted memorandum. Dr. Beitz repeatedly cited Dr. Wilkin with approval in her reconsideration memorandum. She purported to remove his influence by claiming his opinions and reasoning were correct and claiming to have found support for them in the literature. But this process hardly removed Dr. Wilkin's influence; it highlighted the influence. Dr. Beitz all but admits that she reconstructed Dr. Wilkin's reasoning and conclusions by going to the literature for support for them.

The three other persons who participated in the reconsideration process, Drs. Throckmorton, Woodcock and von Eschenbach, each relied on Dr. Beitz's memoranda (and in several instances also cited Dr. Wilkin directly).

B. An Agency Decision That Relies On An Improper Factor Must Be Overturned

Under well-established Supreme Court precedent, an agency decision is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law if the agency relied on factors which Congress did not intended it to consider. *Motor Vehicle*, 463 U.S. at 43.

An agency cannot consider factors Congress did not intend it to consider, such as political and other outside influences, an agency's consideration of relevant factors does not "immunize" the decision; the decision is "invalid if based in whole or in part on pressures emanating from [outside influence.]" *D.C. Fed'n of Civic Assoc's v. Volpe*, 459 F.2d 1231, 1245-46 (D.C. Cir. 1971) (under APA, reversal of agency decision "required because . . . . extraneous pressure intruded into the calculus of considerations"); *Earth Island Institute v. Hogarth*, 494 F.3d 757, 769 (9th Cir. 2007) (vacating agency decision and citing review of the internal memoranda that "shows the agency's decision-making process, which was devised to conduct a scientific analysis [,] was influenced at least some degree by foreign policy considerations rather than science alone[.]"); *Latecoure Int'l v. U.S. Dep't of Navy*, 19

F.3d 1342 (11th Cir. 1994) (vacating award of contract to U.S. company, as opposed to French company, where Secretary of Navy succumbed to political pressure); *Tummino v. Torti*, 603 F. Supp.2d 519 (E.D.N.Y 2009) (under APA, improper outside influence renders FDA decision invalid) (discussing and adopting holdings in *Latecoere* and *D.C. Federation*).

Thus, where an impermissible factor may have been considered:

Even if [the agency] had taken every formal step required by every statutory provision, reversal would still be required.

D.C. Federation, 459 F.2d at 147 (emphasis added); *Tummino*, 603 F. Supp.2d 519 (same).

Here, the FDA acknowledges that reliance on Dr. Wilkin was improper, but failed to remove his influence from its decision-making process. Under well-established law, this requires reversal of its decision.

III. THE APPROPRIATE REMEDY IS TO REVERT TO THE FDA'S CONCENSUS OPINION REACHED PRIOR TO THE TAINT IN THE REVIEW PROCESS

The typical remedy under the APA is to remand the issue for further administrative proceedings. But, numerous courts, including the Ninth Circuit, acknowledge that "a court can order equitable relief or remand with specific instructions" when appropriate. *Earth Island Institute v. Hogarth*, 494 F.3d 757 (9th Cir. 2007) ("generic remand is not appropriate" in light of "government's intransigence"); *Nehemiah Corp. of America v. Jackson*, 546 F. Supp. 2d 830, 847-48 (E.D.Cal. 2008) (disqualification of Secretary of HUD on remand of agency decision "is an appropriate remedy" where he exhibited a closed mind).

In *Gayer v. Schlesinger*, 490 F.2d at 747, the Court found that a security review agency violated the plaintiff's privacy rights during a administrative proceeding. The *Gayer* Court considered the proper remedy in detail, stating that "in view of the history of this case, the proceedings on reconsideration, should they occur,

must be heard by a different Hearing Officer and a different Appeals Board." *Id.* The Circuit Court continued that "any part of the record previously made" that went beyond what the Court had held to be appropriate could not be used. *Id.* The Court also addressed its reasons for imposing these prophylactic measures:

> We set forth these guides for the future without impugning to any degree the rectictude and good faith of the officials who participated in the previous determinations, **but to relieve them of the difficulty of ridding themselves of prior positions taken, in part, on a record which was erroneously prepared in part,** and also, to relieve [the Plaintiff] of the possible side effect of their participation.

Id. (emphasis added).

In this case, the FDA considered the issues presented by Spear's ANDA and reached a Consensus Conclusion in June 2006 that Spear must be required to test sBCC patients. The Record reflects that the determination was reached at an all-hands conference with representatives from all relevant FDA groups, after literally years of consideration of this issue. The Consensus Conclusion was reached before Dr. Wilkin's submission tainted the FDA' s decision-making process.

The appropriate remedy in this case is to remand to the agency with instructions to implement the consensus reached before the taint occurred. Further fact-finding is not necessary. Alternatively, the matter should be remanded with instruction to the FDA to have the matter reconsidered by persons not tainted by the Dr. Wilkin submission and with proper deference to the experts in the FDA's Dermatology Division.

CONCLUSION

For the foregoing reasons, Valeant respectfully requests that the Court grant its Motion for Summary Judgment in full.

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