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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

COLLAGENEX PHARMACEUTICALS, INC.,	)	
Plaintiff,	)	
v.	)	**Civil Action No. 03-1405 (RMC)**
TOMMY G. THOMPSON, Secretary of Health and Human Services, et al.,	)	
Defendants.	)	

MEMORANDUM OPINION

This case presents an interesting conundrum. CollaGenex Pharmaceuticals, Inc. ("CollaGenex") seeks review of a decision by the Food and Drug Administration ("FDA") that its primary medical product, Periostat® ("Periostat"), is an "antibiotic drug" within the meaning of the Food Drug and Cosmetic Act, 21 U.S.C. § 321(jj) ("FDCA"). Because FDA appears to be on the verge of approving generic equivalents of Periostat, CollaGenex seeks a preliminary injunction to forestall that competition, as well as a finding that Periostat is not an antibiotic drug. FDA advised the Court that it intended to act on Monday, July 21, 2003, now extended to later in the week. No administrative record of FDA's decision on Periostat has been submitted. The D.C. Circuit has clearly held that courts should not issue preliminary injunctions without a review of the entire administrative record to determine a plaintiff's likelihood of success on the merits. *See American Bioscience, Inc. v. Thompson*, 243 F.3d 579 (D.C. Cir. 2001). What can be done?

Pending before the Court is CollaGenex's Motion for a Preliminary Injunction, which Secretary Thompson, the Department of Health and Human Services, Commissioner McClellan and

FDA ("Federal Defendants"), along with Intervenor Defendant Mutual Pharmaceutical Company, Inc. ("Mutual"), oppose. The Federal Defendants have also filed a Motion to Dismiss under FED. R. CIV. P. 12(b)(1) and 12(b)(6). Upon consideration of the briefs and oral argument of the parties, the Court finds that CollaGenex has made a strong showing of irreparable harm, that the balance of harms clearly favors CollaGenex, and that the public interest will be served by the issuance of a preliminary injunction. Because FDA is mute on the merits of the case and the Court does not have the administrative record, it cannot perform the normal evaluation of likelihood of success on the merits. Nonetheless, it appearing that CollaGenex has at least a colorable claim under § 321(jj), the Court finds that this is a sufficient showing of likelihood of success under these circumstances. CollaGenex's Motion for a Preliminary Injunction will be granted in part and denied in part and the Federal Defendants' Motion to Dismiss will be granted in part and denied in part pending receipt of the administrative record and its full review.

Background

I. Statutory Framework

New drugs are approved by FDA only after an extensive investigation into their safety and efficacy. An applicant files a new drug application ("NDA") containing detailed data. *See* 21 U.S.C. § 355(j)(7). As described by the parties during oral argument, the process to achieve FDA approval of a new or "pioneer" drug[1] entails a form of negotiation between the applicant and FDA in which the government "gets whatever it wants." It can take tens of millions of dollars and years to develop a new drug and obtain FDA approval.

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[1] The term "pioneer" as applied to a drug means the first approved use of a chemical substance for a specific therapeutic purpose. *See* Donald O. Beers, Generic and Innovator Drugs, § 1.1 (4th ed. 1995).

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984), commonly known as Hatch Waxman. One purpose of Hatch Waxman was to make it easier for drug manufacturers to obtain FDA approval for generic drugs. The generic manufacturer does not have to repeat the expensive and extensive testing associated with obtaining initial approval of an NDA. The generic manufacturer instead may file an abbreviated new drug application ("ANDA"), relying on the testing conducted by the original manufacturer that showed safety and effectiveness. *See Am. Bioscience*, 243 F.3d at 580. The generic manufacturer need only establish that the generic drug is the "bioequivalent" of the brand name drug. 21 U.S.C. §§ 355(j)(2)(A), (j)(8).

In enacting Hatch Waxman, Congress also sought to encourage research and innovation by providing a period of market exclusivity and patent protection for certain pioneer drugs. *See Am. Bioscience*, 243 F.3d at 580. These protections allow recoupment of the costs of development and the approval process without competition from less expensive generic versions of a drug. *See* 59 FED. REG. 50,338 (Oct. 2, 1994). Under Hatch Waxman, certain pioneer drugs enjoy a five-year period of market exclusivity during which no ANDA for a generic copy of the drug may be approved. *See* 21 U.S.C. §§ 355(c)(3)(D), (j)(5)(D)(ii). With respect to patent protection, an NDA applicant must submit the patent number and expiration date of any patents that claim the drug. When a manufacturer files an ANDA to market a generic copy of a drug, the ANDA applicant must certify "(1) that no patent has been filed with the FDA; or (2) that the patent has expired; or (3) that the patent has not expired, but will expire on a particular date; or (4) that the patent is either invalid or the generic drug will not infringe it." *Am. Bioscience*, 243 F.3d at 580. If the ANDA makes a certification under subsection four (commonly called a Paragraph IV certification), the applicant

must provide notice to the patent holder that it has filed the ANDA. *See id.* The patent holder then has a forty-five day period in which to file a patent infringement action. If suit is filed within this period, FDA may not approve the ANDA application until the patent dispute is resolved, or for 30 months, whichever is sooner. *See id.*

Congress enacted the Food and Drug Administration Modernization Act of 1997 ("FDAMA") in November 1997. Prior to its enactment, NDA applications for antibiotic drugs were governed by 21 U.S.C. § 357, and NDA applications for all other drugs were governed by 21 U.S.C. § 355. FDAMA repealed § 357 and requires that NDA applications for antibiotic drugs be submitted under § 355. FDAMA also contains exemption provisions that make antibiotic drugs ineligible for the Hatch Waxman market exclusivity period and patent protections. *See* FDAMA § 125(d)(2). An "antibiotic drug" is defined by FDCA as

> any drug (except drugs for use in animals other than humans) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other drug intended for human use containing any quantity of any chemical substance which is produced by a micro-organism and which has the capacity to inhibit or destroy micro-organisms in dilute solution (including a chemically synthesized equivalent of any such substance) or any derivative thereof.

21 U.S.C. § 321(jj).

After an NDA is awarded, the holder may voluntarily withdraw the drug from sale. FDA then moves the drug to the Discontinued Drug List to provide notice that it has been withdrawn. When this happens, any petition for an ANDA that refers to the prior drug must be accompanied by a petition requesting FDA to determine that the drug was not withdrawn for reasons of safety or efficacy. *See* 21 C.F.R. § 314.122. FDA may not approve the ANDA until FDA makes this

determination. *See* 21 C.F.R. § 314.161(a)(1). If FDA determines the drug was withdrawn for safety or effectiveness reasons, the ANDA will not receive government approval. *See* 21 C.F.R. § 314.162.

II. Factual Background[2]

CollaGenex is a small pharmaceutical company that employs approximately 150 people. Its primary product is a prescription pharmaceutical, Periostat, that is used to treat adult periodontitis. Periostat works by reducing the levels of enzymes, known as collagenase, that destroy the connective tissues that support teeth. The active ingredient in Periostat consists of a 20 milligram ("mg") dose of doxycycline hyclate.

CollaGenex states that it spent nearly twelve years and $70 million dollars developing Periostat. In addition, since 1999, CollaGenex states that it has expended over $87.5 million dollars in direct sales and marketing expenses related to Periostat. Without contradiction, CollaGenex asserts that its only significant revenue comes from sales of Periostat. During 1999, 2000, 2001, and 2002, Periostat accounted for 95%, 84%6, 87%, and 82%, respectively, of the total revenues of CollaGenex, with total revenue during 2002 amounting to $44.5 million. While CollaGenex yielded a net positive income in the last two quarters of 2002, it has experienced net losses each year.

In August 1996, CollaGenex submitted an NDA for 20 mg Periostat capsules under Section 505 of the FDCA, 21 U.S.C. § 355. Shortly thereafter, FDA requested that CollaGenex resubmit its NDA under Section 507 of the FDCA, 21 U.S.C. § 357, the section that governed the review and approval of antibiotic drugs at the time. CollaGenex protested, asserting that Periostat did not meet

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[2] The facts are taken from the Complaint, the parties' briefs and supporting affidavits, and representations made by counsel in open court.

the statutory definition of an antibiotic drug. FDA advised CollaGenex that it could pursue its claim and postpone approval of its application or submit the NDA as an antibiotic drug and contemporaneously attempt to get it re-classified. CollaGenex elected to submit the NDA as an antibiotic drug under § 357 and concurrently pursue its objections during the NDA review. On September 11, 1997, CollaGenex submitted a Request for Designation to the FDA Ombudsman asking that Periostat be designated a nonantibiotic drug under 21 U.S.C. § 355, rather than an antibiotic drug under 21 U.S.C. § 357. Two years after the application process began, FDA approved the NDA for Periostat in September 1998. The approval stated, without explanation, that Periostat is subject to the exemption provisions of FDAMA § 125(d)(2), and not eligible for market exclusivity and patent protections available to drugs approved under 21 U.S.C. § 355. In 2001, the FDA approved an NDA permitting CollaGenex to market Periostat tablets.

CollaGenex voluntarily stopped distributing and marketing Periostat capsules in August 2001. CollaGenex wrote to FDA in September 2001 to withdraw the NDA for Periostat capsules, and submitted the requisite paperwork under 21 C.F.R. § 314.81(b)(3)(iii). FDA neither published a notice in the Federal Register announcing this withdrawal nor moved the capsules to the "Discontinued Product List."[3] On July 10, 2002, CollaGenex submitted a Citizen Petition to FDA and a Petition for Stay of Action. The Citizen Petition requested that FDA not approve any ANDA for Periostat capsules until FDA determined that the capsules had not been withdrawn for safety and effectiveness reasons, that FDA refuse to receive or approve any ANDA for a generic version of Periostat capsules not accompanied by a petition seeking a determination regarding whether the

[3] This list contains all the products that have been discontinued from marketing and is one of the places where a company would look to determine if it needed to attach a safety or effectiveness petition to its ANDA application.

capsules were withdrawn for safety or effectiveness reasons, that FDA immediately move the capsules to the Discontinued Product List, and that FDA publish a Federal Register notice announcing the withdrawal of the NDA for Periostat capsules. In the Stay Petition, CollaGenex requested that FDA not to take any action on any ANDA for a generic version of Periostat until it had decided the Citizen Petition. FDA has yet to issue a decision on these Petitions.

FDA's Chief Counsel, Daniel E. Troy, has encouraged companies that are considering filing suit against FDA to "lay [their] cards on the table" by meeting with him and discussing the potential suit. *See Unsupported Claims Should Be Brought to FDA by Industry*, F-D-C Rep. ("The Tan Sheet"), Oct. 14, 2002, at 11. Pursuant to this approach, counsel for CollaGenex met with him in January 2003 to discuss FDA's determination that Periostat is an antibiotic drug and CollaGenex's contemplated federal court litigation. Mr. Troy suggested that CollaGenex submit a letter following the meeting rather than file a citizen petition or a petition for stay of action, outlining its arguments concerning the classification of Periostat. CollaGenex complied with this request on January 21, 2003, submitting a lengthy letter explaining its arguments that Periostat is not an antibiotic drug. *See* Federal Defendants' Memorandum in Support of its Motion to Dismiss and in Opposition to Plaintiff's Motion for Preliminary Injunction, Attachment A at 1 ("Federal Opposition"). In this letter, CollaGenex noted that it had delayed filing suit to enable the parties to resolve the matter short of litigation. It also requested ten business days notice if FDA were going to approve a pending ANDA, in order to allow CollaGenex time to initiate litigation. *See id.* at 12.

In the meantime, at least two companies, Intervenor Mutual and West-ward Pharmaceutical Corporation, have submitted an ANDA to market a generic version of Periostat.[4] FDA has not acted on these applications yet, but has represented to the Court that action is imminent.

Analysis

I. Ripeness

FDA rests its case for dismissal almost entirely on the issue of ripeness. As to the question of whether Periostat is an "antibiotic drug," FDA presents the argument as encompassing two separate points. First, FDA asserts that CollaGenex has not exhausted its administrative remedies because it submitted a January 2003 request for reconsideration of FDA's 1998 determination that Periostat is an antibiotic drug, which is still under review. *See Stone v. INS*, 514 U.S. 386, 392 (1995) (Under the APA, "filing of a motion to reconsider renders the underlying order nonfinal for purposes of judicial review."); 21 C.F.R. § 10.45(b). Second, FDA argues that CollaGenex has not been harmed by any Agency action inasmuch as FDA has not yet approved any ANDA. *See Pfizer Inc. v. Shalala, et al.*, 182 F.3d 975, 978 (1999) (FDA acceptance of ANDA for processing not a final agency action). These arguments on the initial counts of the Complaint are not persuasive.

However, Count V of the Complaint is premature and will be dismissed. That Count relates to a September 2001 letter to FDA from CollaGenex requesting that FDA withdraw the NDA for Periostat capsules and a July 2002 Citizen Petition and Stay Petition requesting that FDA not approve any ANDA for Periostat capsules until FDA has determined that the capsules were not withdrawn for safety and effectiveness reasons. FDA has not yet issued responses to these requests. Without final agency action, neither claim is ripe for review. *Reliable Automatic Sprinkler Co. v.*

[4] CollaGenex is presently proceeding against West-ward in a patent infringement action.

CPSC, 324 F.3d 726, 731 (D.C. Cir. 2003) (dismissal under Fed. R. Civ. P. 12(b)(6) when there is no final agency action). Therefore, the Federal Defendants' Motion to Dismiss is granted with respect to Count V.

FDA's "failure to exhaust" argument categorizes a January 2003 letter from CollaGenex to Chief Counsel Troy as a request for reconsideration. CollaGenex describes its January 2003 letter as an effort, in response to speeches from the Chief Counsel of FDA, to approach the Agency prior to suit, lay out its theories of litigation, and potentially achieve a settlement.[5] The Court agrees and finds that the January 2003 letter was not a request for reconsideration. It specifically stated that it was submitted "in letter form rather than as a citizen petition and related petition for stay of action." *See* Federal Opposition, Attachment A at 1. More significantly, despite the frequent use of the word "request" in the letter, it stated in the conclusion that

> CollaGenex has delayed filing a lawsuit in Federal Court solely to provide a period of time to resolve these issues without resort to litigation. . . . [I]f FDA believes that it must approve the West-Ward ANDA imminently, [we ask for] at least ten business days notice so that CollaGenex will have the opportunity to initiate litigation on the issue . . . .

Id. at 12. These statements demonstrate that the January 2003 letter was intended to speak frankly with FDA in an effort to avoid litigation and was not intended to be a request for reconsideration.

The *Pfizer* argument presented by FDA appears at first blush to have greater significance. In *Pfizer*, the drug company sought to prevent FDA from approving an ANDA without Pfizer's extended release mechanism. Citing *Texas v. United States*, 523 U.S. 296, 300 (1998), for the

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[5] Memorandum of Points and Authorities in Reply to Federal Defendants' Opposition to Plaintiff's Motion for a Preliminary Injunction at 3 ("FDA's Chief Counsel has invited companies that are considering suing FDA to meet with him first to 'lay [the] cards on the table.'") (hereafter "CollaGenex's Reply"); *see also, e.g.*, *Unsupported Claims Should Be Brought to FDA By Industry*, F-D-C Rep. ("The Tan Sheet"), Oct. 14, 2002, at 11.

proposition that "[a] claim is not ripe for adjudication if it rests upon contingent future events that may not occur as anticipated, or indeed may not occur at all," the D.C. Circuit agreed that Pfizer's claim was premature because FDA had not approved the ANDA and might not do so. FDA argues that this proposition applies and bars the CollaGenex suit as premature.

The difference here is that CollaGenex appeals a final agency decision of 1998 relating to FDA's determination that Periostat is an antibiotic drug. If FDA erred in its 1998 determination, then CollaGenex would be entitled to the protections from generic drugs that are available under Hatch Waxman. Its effort to prevent approval of Mutual's ANDA is therefore not an attack on the ANDA itself – which is not *quite* final but, according to government counsel, will be after Wednesday, July 23, 2003 – but rather an appeal from the 1998 final agency decision and its present-day consequences.

It is easy to agree with FDA and Mutual that CollaGenex could have filed this appeal at any time between 1998 and the present and that its timing has created an emergency that might have been avoided. The Court cannot reasonably object, however, to a litigant who did not run to the courthouse at the first opportunity and who hoped, perhaps naively, that such litigation would never be necessary. CollaGenex has filed suit over the 1998 final agency decision within the six years of the statute of limitations and has a right to have its case heard and decided. This lawsuit is not premature; rather, it is fully ripe for decision.

II. Preliminary Injunction

A preliminary injunction may only be granted when a party shows a substantial likelihood of success on the merits, a balance of harms that favors the movant, irreparable harm if no injunction is granted, and service in the public interest from an injunction. *See Katz v. Georgetown Univ.*, 246

F.3d 685, 687-88 (D.C. Cir. 2001); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998). A court balances the four factors and a particularly strong showing on one or more can outbalance a weaker showing on another. *CityFed Fin. Corp. v. Office of Thrift Supervision*, 58 F.3d 738, 747 (D.C. Cir. 1995); *Wash. Metro. Area Transit Comm'n v. Holiday Tours*, 559 F.2d 841, 843-45 (D.C. Cir. 1977). Here, the Court concludes that CollaGenex has at least a legitimate claim on the merits and that the other three factors strongly support a preliminary injunction.

1. Likelihood of success on the merits

The analysis of CollaGenex's likelihood of success is influenced by FDA's present litigating posture. Since the Agency asserts that the January 2003 letter constituted a request for reconsideration, it has been able to argue that the case is not ripe and to avoid almost all comment on the substantive issue of whether Periostat is an antibiotic drug. In theory, as explained by FDA counsel, that issue is under active reconsideration. Only when FDA counsel told the Court, at the close of oral argument, that FDA's decisions on these matters would issue on Monday, July 21, 2003,[6] did counsel also admit that it is unlikely that FDA would change its determination that Periostat is an antibiotic drug. Nonetheless, FDA argues that CollaGenex has little likelihood of success on the merits because FDA's future determination that Periostat is an antibiotic drug will be entitled to great deference so that the Court would have no reason to overturn it. *See* Federal

[6] FDA counsel assured the Court, at the beginning of oral argument on Wednesday, July 16, 2003, that FDA would only issue its decisions "after Friday" in an effort to allow the Court to rule on this matter. At the end of the argument, when pressed by the Court as to when FDA really would act, FDA counsel conceded that FDA intended to act on Monday, July 21. The Court agrees that Monday, July 21, is "after Friday," July 18. However, the lack of a forthright statement on the planned schedule when specifically asked by the Court was little short of gamesmanship and hide-the-ball which is unbecoming to a federal official or an officer of the court. Only reluctantly did FDA, when its actual schedule was revealed, agree to withhold action until after Wednesday, July 23, 2003, so that this matter might be addressed here.

Opposition at 16 ("Once FDA makes its final decisions on whether Periostat should be designated an antibiotic . . ., CollaGenex would be unlikely to succeed in showing that FDA's decisions are arbitrary and capricious."); *see also* 5 U.S.C. § 706(2)(A) (standard of reversal under APA is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.") FDA also argues that it is regularly "accorded particular deference when its decisions are based on evaluation of scientific information within its area of technical expertise." Federal Opposition at 17; *see also Troy Corp. v. Browner*, 120 F.3d 277, 283 (D.C. Cir. 1997) (Courts "review scientific judgments of the agency 'not as the chemist, biologist, or statistician that we are qualified neither by training nor experience to be, but as a reviewing court exercising our narrowly defined duty of holding agencies to certain minimal standards of rationality.") (quoting *Ethyl Corp. v. EPA*, 541 F.2d 1, 36 (D.C. Cir. 1976)).

Additionally, FDA and Mutual argue that the Court cannot rule on the motion for a preliminary injunction because there is no administrative record on which to base its decision. *American Bioscience* appears to support this argument. In *American Bioscience*, the plaintiff sought a preliminary injunction to prevent FDA from approving an ANDA. Without the formal administrative record before it, the district court had made findings of fact as to the bases for FDA action based on "the parties' written or oral representations." *Am Bioscience*, 243 F.3d at 582. The Court of Appeals reversed, holding that "the court, before assessing American Bioscience's probability of success on the merits, should have required the FDA to file the administrative record and should have determined the grounds on which the FDA granted Baker Norton's application." *Id.* at 582. *American Bioscience* based its holding on *Citizens to Preserve Overton Park v. Volpe*,

Court means a "claim that is legitimate and that may reasonably be asserted given the facts presented and the current law." BLACK'S LAW DICTIONARY 240 (7th Ed. 1999); *see also Cuomo v. United States Nuclear Regulatory Comm'n*, 772 F.2d 972, 974 (D.C. Cir. 1985) ("A stay may be granted with either a high probability of success and some injury, *or vice versa*." (emphasis in original)) Without the administrative record from the 1998 decision, or even any input from the FDA, the Court is left to the use of the English language to determine if CollaGenex has made a colorable claim.

The place to start, as with any statutory question, is the language of the statute itself. The FDCA defines an antibiotic drug at 21 U.S.C. § 321(jj):

> The term "antibiotic drug" means any drug (except drugs for use in animals other than humans) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other drug intended for human use containing any quantity of any chemical substance which is produced by a micro-organism and which has the capacity to inhibit or destroy micro-organisms in dilute solution (including a chemically synthesized equivalent of any such substance) or any derivative thereof.

No one argues that Periostat is one of, or a derivative of one of, the antibiotic drugs specifically identified in § 321(jj). Nor is its intended use for humans under question. Therefore, as relevant here, the statute provides:

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and, instead, sent it as an attachment to an email to the Clerk's Office. The email was sent after 11 pm on Friday, July 11, 2003, when there was no one working in the Clerk's Office to transfer the materials from email to ECF. That transfer occurred on Monday, July 14, 2003, when the Clerk's Office opened. As a result, neither CollaGenex nor FDA was able to read or respond to the substantive arguments in Mutual's brief and attachments prior to the oral argument on July 16, although CollaGenex disputed them before the Court. Because of this accident and because the Court cannot determine whether Periostat is or is not an antibiotic drug without a full administrative record, Mutual's arguments on these points will be disregarded.

> The term "antibiotic drug" means any drug . . . containing any quantity of any chemical substance which is produced by a micro-organism and which has the capacity to inhibit or destroy micro-organisms in dilute solution (including a chemically synthesized equivalent of any such substance) . . . .

This language might appear daunting to non-scientists but it is simpler than it first appears. WEBSTER'S defines "antibiotic" as "a substance produced by a microorganism (as a bacterium or a fungus) and in dilute solution having the capacity to inhibit the growth of or kill another microorganism (as a disease germ)." WEBSTER'S THIRD NEW INT'L DICTIONARY UNABRIDGED 93 (2002). Asked by the Court, CollaGenex, FDA and Mutual all defined an antibiotic as having the two characteristics identified by WEBSTER'S: 1) produced by a microorganism and 2) having the capacity to inhibit or kill microorganisms. With this assistance from Mr. Webster and the parties, the Court can parse the statute to mean:

> The term "antibiotic drug" means any drug . . . containing any quantity of [an antibiotic] (including a chemically synthesized equivalent of any [antibiotic]) . . ."

Thus, an "antibiotic drug" must contain an "antibiotic," which, by definition, 1) is produced by a microorganism and 2) has the capacity to inhibit or kill microorganisms. The active ingredient in Periostat is doxycycline hyclate 20 mg. It is agreed by all that doxycycline hyclate at 50 mg or higher concentrations is an "antibiotic drug" because it contains an "antibiotic" that is produced by a microorganism and has the capacity to kill microorganisms. CollaGenex asserts that doxycycline hyclate 20 mg is produced by a microorganism but does not have the capacity to kill microorganisms because the concentration of doxycycline is too low to have that ability or to achieve that result. FDA seems to agree: The Dental Officer reviewing CollaGenex's application for approval of Periostat concluded that the drug was "not antimicrobial at this [20 mg] dosage." Robert A. Ashley

Decl. at ¶ 31(hereafter "Ashley Decl."); Memorandum of Points and Authorities in Support of Plaintiff's Motion for a Preliminary Injunction (hereafter "CollaGenex's Brief"), Att. 12 at 1. The Review and Evaluation of Pharmacology and Toxicology Data said that the proposed dosage for Periostat was "apparently below the threshold for antibacterial effects." Ashley Decl. at ¶ 32; CollaGenex's Brief, Att. 13 at 4. The package insert for Periostat, which was extensively negotiated between CollaGenex and FDA according to both parties, states that "[t]he dosage of doxycycline achieved with this product during administration is well below the concentration required to inhibit microorganisms commonly associated with adult periodontitis." Ashley Decl. at ¶ 26; CollaGenex's Brief, Att. 7 at 1.

Per § 321(jj), an antibiotic drug must contain an antibiotic. An antibiotic must have the *capacity* to kill (or inhibit) microorganisms. Doxycycline at 20 mg does not have the capacity to kill or inhibit microorganisms – it is too weak. Mutual argues that the statute provides that it takes only "any quantity" of an antibiotic to constitute an antibiotic drug and that, as long as doxycycline has antibiotic capacity at some concentrations, it is an antibiotic drug at all concentrations. FDA, having taken the position that this is all premature, offers no opinion. Mutual's reading of the statute may align with the silent FDA but it is not the only reading. Thus, while it is true that "any quantity" of an antibiotic in a drug will make that drug an "antibiotic drug," the drug still must contain some amount of an "antibiotic,"*i.e.*, a chemical substance 1) produced by microorganisms and 2) with the capacity to kill (or inhibit) microorganisms. At a 20 mg concentration, doxycycline does not have

the capacity to kill or inhibit microorganisms and, arguably, does not therefore meet the definition of an "antibiotic" or an "antibiotic drug."[8]

The Court hastens to say that its conclusion arises only from a reading of the statutory language, without the benefit of the administrative record or even an articulated position from FDA. FDA experts apparently reached a different conclusion in 1998, which will be subject to review and deference as warranted when the administrative record is before the Court. *See Chevron U.S.A. v. Nat'l Res. Def. Council, Inc.*, 467 U.S. 837 (1984). Since FDA has not filed the record at this time, however, it is enough to say that CollaGenex has a colorable claim that Periostat is not an antibiotic drug and therefore has made a sufficient showing of likelihood of success.

2. Balance of Harms

To be sure, CollaGenex has shown that it could suffer devastating losses that would affect its viability. The harm that the defendants would suffer is minimal. FDA argues that its administrative process for regulating drugs would be disrupted, but that point of view is dependent on FDA's belief that CollaGenex seeks review of the alleged motion for reconsideration, which the Court has rejected. CollaGenex seeks review of FDA's final agency decision from 1998 and that review is customary, normal and not disruptive of the administrative process. Mutual, which has a pending ANDA, may suffer some harm from entry of an injunction because the injunction will delay its ability to bring a generic version of Periostat to market. Given Mutual's large size, resources, and

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[8] Over time, patients who take antibiotics can develop resistance to them making their next disease more difficult to treat. Therefore, it would be reasonable for Congress to require that drug manufacturers advise patients of the presence of antibiotics in their medicine, regardless of whether the antibiotic (which is produced by microorganisms and has the capacity to kill or inhibit microorganisms) constitutes only a very small percentage of the total medication. CollaGenex asserts that the concentrations of doxycycline in Periostat are too low to contribute to antibiotic resistance.

essentially limited investment in its generic drug, in contrast to CollaGenex's small size, limited product line, and significant investment in Periostat, the potential harm to Mutual is comparatively minimal. The Court finds that the balance of harms clearly and substantially weighs in favor of an injunction so that the Court can receive the full administrative record and make a determination on it.

3. Irreparable Harm

CollaGenex depends on Periostat for over 80% of its revenue. Approval of one or more ANDAs is imminent; in fact, "Mutual believes [its ANDA] is ready for approval." Memorandum of Intervenor-Defendant Mutual Pharmaceutical Company, Inc. in Opposition to Plaintiff's Motion for Preliminary Injunction at 1. Mutual has already begun a web-based marketing effort for its generic version of Periostat, offering a discount for early orders which could otherwise go only to CollaGenex. It plans to "ship product to [purchasers] upon receipt of FDA approval." Gallagher Supp. Decl. at ¶ 1, Exh. 1 at 2. Thus, it appears that Mutual may already be eroding CollaGenex's market share.

FDA argues that no harm is "imminent" to CollaGenex. There are two problems with the argument. First, it is advanced, as are all FDA arguments, from the point of view that this lawsuit is premature. FDA suggests that CollaGenex could and should act only if and when FDA actually approves an ANDA. But if CollaGenex is correct that Periostat is not an antibiotic drug and that FDA's 1998 determination was incorrect, it should not be facing the competition from one or more ANDAs at this time. In fact, Mutual is already working to build its market share so that approval of its ANDA would not initiate the potential harm to CollaGenex; it is happening now. Second, the argument ignores the evidence proffered by CollaGenex that rapid erosion of branded drug sales can

occur when a generic enters the market. It cites industry publications to demonstrate that generic Prozac achieved 59% market penetration of total prescriptions for one dosage strength and 70% of new prescriptions for another dosage strength within one month of launch. Within two weeks of availability of a generic version of Astra's drug Zestril, Merck-Medco mail order pharmacy apparently achieved 91% generic conversion. Megestrol is said to have achieved 75% market share within six months. *See* CollaGenex's Reply at 11-12.

These figures are not surprising in the modern world where individual doctors and patients no longer make many prescription choice decisions. Those decisions are often dictated by insurers, who insist on cheaper, generic drugs as soon as they are available unless a physician can demonstrate a medical need for the pioneer drug. It is not at all difficult to foresee that CollaGenex's market position would collapse as soon as one or more generic drugs became available. CollaGenex would lose its head start in the market and its continued viability would be at issue. It could never recoup from FDA any losses that would occur. Its David-and-Goliath size comparison to Mutual could make competition between the two a very uneven match.[9] These are the kinds of circumstances in which irreparable harm has been found. *See Mova Pharm Corp. v. Shalala*, 140 F.3d at 1066 n.6 ("[T]he district court found that Mova would be harmed by the loss of its 'officially sanctioned head start' and that Mova's small size put it at a particular disadvantage. This suffices to show a severe economic impact to Mova."); *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 29 (D.D.C. 1997) ("While the injury to plaintiffs is 'admittedly economic,' there is 'no adequate compensatory

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[9] Mutual enjoyed over $290 million in sales of generic drugs in one year alone. United Research Laboratories/Mutual Pharmaceutical Sales Top $290 Million, Health and Medicine Week, at 16, March 10, 2003; *see also* CollaGenex Reply at 14. Counsel for Mutual informed the Court that Mutual manufactures only generic drugs and does no initial research or new-drug development.

or other corrective relief' that can be provided at a later date, tipping the balance in favor of injunctive relief.") (quoting *Hoffman Laroche Inc. v. Califano*, 453 F. Supp. 900, 903 (D.D.C. 1978)).

The Court finds that CollaGenex has shown substantial and convincing evidence that it would suffer irreparable harm without a preliminary injunction.

4. Public Interest

FDA and Mutual argue that the public interest is served by ready access to less-expensive generic drugs and that the Court should not prevent FDA approval of Mutual's ANDA. CollaGenex argues that the public has an interest in its ability to continue research and development on new disease treatments.

Congress has determined that those companies that engage in research and new-drug development should have certain protections from competition when a drug is first introduced to the market place. These protections are built into the governing law to provide an inducement to the lengthy and expensive research and development process by assuring a legitimate profit before competitors can intrude. Without these inducements, there would be very little reason for a research company to invest millions of dollars only to have another company re-formulate the same drug, submit an ANDA, avoid the costs of development, charge less for its product, and assume dominance in the market. Thus, the barriers to competition that Congress has erected are in the public interest because they encourage the development of innovative drugs by ensuring a period of market exclusivity. As stated above, CollaGenex has made a sufficient showing of likelihood of success, given the awkward posture of this suit. For this reason, as well as the strength of the showing on balance of harms and irreparable harm, the countervailing public interest in the