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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

COLLAGENEX PHARMACEUTICALS, INC.,)
)
Plaintiff,)
)
v.) Civ. Case No. 03-01405 (RMC)
)
TOMMY G. THOMPSON, Secretary)
of Health and Human Services, DEPARTMENT)
OF HEALTH AND HUMAN SERVICES,)
MARK B. McCLELLAN,)
Commissioner of Food and Drugs, and)
FOOD AND DRUG ADMINISTRATION,)
)
Defendants,)
)
MUTUAL PHARMACEUTICAL)
COMPANY, INC.,)
)
Intervenor-Defendant,)
)
and)
)
WEST-WARD PHARMACEUTICAL CORP.,)
)
Intervenor-Defendant.)

DECLARATION OF MURRAY M. LUMPKIN, M.D.

1. I am currently the Principal Associate Commissioner of the United States Food and Drug Administration (FDA), in Rockville, Maryland.
2. From May 1994 until September 2000, I was the Deputy Director for Review Management in the Center for Drug Evaluation and Research (CDER) at FDA. In that capacity, I oversaw the offices within CDER that were responsible for reviewing marketing authorization applications for products under CDER's jurisdiction. In addition, I was responsible for regulatory policy decisions related to the oversight functions of these offices. One of those policies included whether the drug described in

the marketing authorization application was an “antibiotic drug,” as described in the 1997 FDA Modernization Act (FDAMA), and thus subject to the exemption provisions contained in section 125(d)(2) of Title I (“the exemption provisions”) of FDAMA. I made these decisions based upon the scientific and regulatory standards contained in the Federal Food, Drug, and Cosmetic Act (FFDCA), the implementing regulations, FDA precedent, and my knowledge and experience.

The Periostat Application

3. In mid-September 1997, Steven Unger, in the office of the Ombudsman in the FDA Commissioner’s Office, forwarded to CDER a letter to Ms Amanda Bryce Norton (then the FDA Chief Mediator and Ombudsman) from Edward Korwek at Hogan and Hartson. In this pre-FDAMA submission, Mr. Korwek, on behalf of CollaGenex Pharmaceuticals, Inc. requested that FDA “designate” Periostat (doxycycline hyclate capsules) 20 mg (NDA # 50-774) as subject to the provisions of section 505(b) of the FFDCA. (Attachment 1) The letter was referred from the Ombudsman’s Office to CDER for a decision. (Attachment 2)

4. In July 1998, I received from Nancy L. Buc, also on behalf of CollaGenex, a letter, dated July 8, 1998, reviewing the reasons she believed Periostat should not be regulated as an antibiotic drug, and discussing the application of FDAMA, which had been passed in November 1997, to the Periostat decision. (Attachment 3)

5. FDA approved Periostat on September 30, 1998. The approval letter stated that the application is subject to the exemption provisions contained in section 125(d)(2) of Title I of FDAMA. (Attachment 4)

6. In the July 1998 letter, Ms Buc basically argues that Periostat should not be classified as an “antibiotic” because it is not intended to kill or inhibit microorganisms and that it does not kill or inhibit microorganisms. My reading of her letter is that she argues that the phrase “which has the capacity to inhibit or destroy microorganisms in dilute solution” refers back to the words “any quantity” earlier in the statutory definitional sentence. As she maintains that the quantity of doxycycline in Periostat is not sufficient to kill or inhibit microorganisms, she argues that Periostat does not meet the statutory definition. In addition she argues that Periostat does not meet the standard medical or consumer concept of an “antibiotic” and would therefore it would be “confusing” for FDA to conclude that it is such. On this last point, as explained further below, FDA does not claim that this product is an “antibiotic” in the medical or consumer sense of the term. Rather, FDA concluded that it was a product that contained a substance that met the *statutory* definition for drugs that were to be regulated as antibiotic drugs under the provisions of the FFDCA.

7. I do not recall whether I documented the reasons I concurred with the review division’s initial decision to regulate Periostat as an antibiotic drug as defined in the FFDCA. However, I understand that CDER has not been able to locate any written documentation from me from 1998 on this matter.

8. The determination to regulate Periostat as a drug that met the statutory definition of an antibiotic drug, and was thus subject to the exemption provisions of FDAMA, was not a particularly difficult decision. There was already a long history of FDA regulating products containing the substance “doxycycline” under the previous Section 507 antibiotic provisions of the FFDCA. Our reading of the plain language of Section 507 is

that Congress clearly intended the provisions of Section 507 to apply (as the statutory definition reads) to “any drug ... containing any quantity of any chemical substance” which meets the two hurdles of (a) production by a microorganism and (b) having the capacity to inhibit or destroy microorganisms in dilute solution. In 1997, Congress reaffirmed this definition in FDAMA. In FDA's opinion and practice the phrase “... which has the capacity to inhibit or destroy microorganisms” refers in the definition sentence to the “chemical substance” and not to “any quantity.” This interpretation, FDA believes, is consistent with the fundamental historical purpose and intent of the original 507 section of the FFDCa.

9. Congress enacted Section 507 at a time when the production of medicines from fermentation involving living microorganisms was quite new and still rather rudimentary. Congress enacted Section 507 to differentiate products manufactured in this manner in order to help assure release of safe production batches. Because it was manufacturing safety concerns that Congress was trying to address with this provision, Congress was quite rational in applying the two characteristics that define the scope of Section 507 to the fundamental *substance* produced by the manufacturing process and not to individual products made subsequently with that manufactured substance. Likewise we believe it rational that Congress intended a *substance* to either fall under these provisions or not to fall under these provisions. Again, given that these provisions were enacted to address safety concerns during manufacturing, it could not follow that a substance manufactured by this methodology would, under certain circumstances, fall under this Section and in certain circumstance would not fall under this Section.

10. Because the medical therapeutic intended use of the substance or the popular perception of what it means for a drug to be an antibiotic has never been a part of the statutory definition in Section 507, FDA has a long history of regulating drug products under Section 507 if the substance in the product meets the 507 statutory definition, even if the product is not used to treat infectious diseases (examples are certain cancer therapies or immunosuppressive therapies). This longstanding practice is further evidence of the FDA's interpretation that the 507 statutory definitions apply to *substances*.

11. Before this specific marketing authorization application was submitted, products containing the substance "doxycycline" had a long history of being regulated under the 507 provisions. This substance clearly is produced by a microorganism and in dilute solution it inhibits microorganisms; in fact, it has FDA approval for marketing with just such an indication.

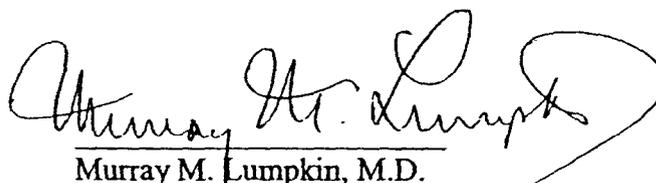
12. As the product in application 50-774 contains doxycycline ("at any quantity") and is intended for use in man, it was the FDA's decision that the product must be regulated as an antibiotic drug, as defined in the FFDCA, consistent with our regulation of all other doxycycline-containing products. (Attachment 5) In this case, the status of the product as an antibiotic drug made it subject to the exemption provisions of FDAMA.

13. For the foregoing reasons, CDER approved Periostat under Section 505, but subject to the exemption provisions of FDAMA, reaffirming the principle that the intended use of the drug product and the question of the ability of the concentration of doxycycline in this specific product to inhibit microorganisms were not relevant under

the statute's definition provisions that determine the scope of products to be regulated under the old 507 provision and under the exemption provisions of FDAMA.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Executed this 13rd day of September 2003, at Rockville, Maryland.

A handwritten signature in cursive script, appearing to read "Murray M. Lumpkin". The signature is written in black ink and is positioned above the printed name.

Murray M. Lumpkin, M.D.
Principal Associate Commissioner
United States Food and Drug Administration