ANDA 214934

TENTATIVE APPROVAL

Nexus Pharmaceuticals, Inc.
400 Knightsbridge Parkway
Lincolnshire, IL 60069
Attention: Carrie Underhill Barnett
Director, Regulatory Affairs

Dear Carrie Underhill Barnett:

This letter is in reference to your abbreviated new drug application (ANDA) for Minocycline for Injection USP, 100 mg per vial (Single-Dose Vial), approved on July 22, 2022, pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

On October 7, 2022, the United States District Court for the District of Columbia issued an Order and an Opinion finding, among other things, that the documentation Nexus Pharmaceuticals, Inc. (Nexus) submitted to ANDA 214934 under 21 CFR 314.95(e) did not qualify as "adequate documentation of the date of receipt" of the notice described in section 505(j)(2)(B) of the FD&C Act.[1] The court remanded the case to FDA "for further action consistent with this Order and the contemporaneously issued Memorandum Opinion, including a determination of the date notice of Nexus's Paragraph IV certification was received for purposes of 21 U.S.C. § 355(j)(5)(B)(iii)."[2]

As directed in the court's October 7, 2022 Order and Opinion, we have determined that, based on the facts before us, including multiple submissions to FDA from or on behalf of the new drug application (NDA) holder and patent owner, Melinta Therapeutics, LLC, and its wholly owned subsidiary, Rempex Pharmaceuticals, Inc., including a citizen petition received on January 11, 2023 (Docket No. FDA-2023-P-0127), notice of Nexus' paragraph IV certifications was received on March 31, 2021.[3] Therefore, FDA is issuing a **tentative approval** of Nexus's ANDA 214934 for Minocycline for Injection USP, 100 mg per vial (Single-Dose Vial).

This determination is based upon information available to the Agency at this time (e.g., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the FD&C Act.

The reference listed drug (RLD) upon which you have based your ANDA, Minocin for Injection, 100 mg/vial, of Rempex Pharmaceuticals Inc. (Rempex), is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
9,084,802 (the '802 patent)	May 12, 2031
9,278,105 (the '105 patent)	May 12, 2031

Your ANDA contains paragraph IV certifications to each patent under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Minocycline for Injection USP, 100 mg per vial (Single-Dose Vial), under this ANDA. The Agency has determined that the requirements of section 505(j)(2)(B) of the FD&C Act have been met. Litigation was initiated within the statutory 45-day period against Nexus for infringement of the '802 and '105 patents in the United States District Court for the Northern District of Illinois [Melinta Therapeutics, LLC et al v. Nexus Pharmaceuticals, Inc., Civil Action No. 21-cv-02636 (consolidated)].

Therefore, final approval cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii) of the FD&C Act,

   b. the date the court decides[4] that the '802 and '105 patents are invalid or not infringed (see sections 505(j)(5)(B)(iii)(I), (II), and (III) of the FD&C Act), or

   c. the '802 and '105 patents have expired, and

2. The Agency is assured there is no new information that would affect whether final approval should be granted.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

RESUBMISSION

To request final approval, please submit an amendment titled "FINAL APPROVAL REQUESTED" with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 3 months for Agency review. Accordingly, such a request for final approval should be

submitted no later than 3 months prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in the status of the manufacturing and testing facilities' compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available Agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. As part of this consideration, applicants should monitor any changes to the RLD that occur after tentative approval, including changes in labeling, patent or exclusivity information, or marketing status. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a "FINAL APPROVAL REQUESTED".

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[5] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dosage forms or active pharmaceutical ingredients manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be

deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact LCDR Daniil Marchuk, Regulatory Project Manager, at (240) 402-4322.

Sincerely yours,

{See appended electronic signature page}

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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[1] Melinta Therapeutics, LLC v. U.S. Food and Drug Administration, No. 22-cv-2190, Dkts. 33 and 34 (D.D.C. Oct. 7, 2022).
[2] Melinta Therapeutics, LLC v. U.S. Food and Drug Administration, No. 22-cv-2190, Dkt. 33 at 1.
[3] See June 2, 2023 Response to Melinta Therapeutics, LLC Citizen Petition, Docket No. FDA-2023-P-0127, available at https://www.regulations.gov/docket/FDA-2023-P-0127.
[4] This decision may be either a decision of the district court or the court of appeals, whichever court is the first to decide that the patent is invalid or not infringed.
[5] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SARAH G KURTZ
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