DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue Stoneham, MA 02180 (781)587-7500 Fax:(781)587-7556	4/24/2017-5/4/2017* FEI NUMBER 3008477155

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Amarpreet S. Sawhney , Chairman/President/CEO	
FIRM NAME Ocular Therapeutix Inc.	STREET ADDRESS 36 Crosby Dr Ste 101
CITY, STATE, ZIP CODE, COUNTRY Bedford, MA 01730-1402	TYPE ESTABLISHMENT INSPECTED Sterile Drug Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

OBSERVATION 1

Written records are not always made of investigations into unexplained discrepancies.

Specifically, Your firm failed to investigate the nature of particulate matter that has been found in manufactured drug product. For example, Dextenza (Dexamethasone Punctum Plug 0.4mg) Lots (b) (4) which had 224 plugs rejected due to an unknown particulate matter, (b) (4) which had 45 plugs rejected due to unknown particulate matter, and (b) (4) which had 37 plugs rejected due to unknown particulate matter, were released for intended commercial use on 12JAN2017 without an investigation or risk assessment on drug quality or product safety. Your firm initiated an investigation on 28APR2017 after product release when you noted that particulate matter in these lots appeared inclusive of aluminum.

Particulate matter has been noted in 10/23 lots (intended use clinical, R&D, stability,etc.) manufactured from FEB2016 to date. The remaining (b) lots were scrapped prior to the visual inspection therefore their particulate status remains unknown.

Particulates were not logged as product defects prior to FEB2016, therefore lots released prior to that date, such as clinical trial lots [redacted], released [redacted], respectively and used in human clinical trials are unknown with respect to particulate status; Lots [redacted] released and intended for human clinical trials [redacted] and [redacted] are also unknown with respect to particulate status.

AMENDMENT 1

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Nealie C Newberger, Lead Investigator 5/4/2017 X Nealie C Newberger Nealie C Newberger Lead Investigator Signed by: Nealie C. Newberger -S	5/4/2017

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OBSERVATION 2

Written production and process control procedures are not followed in the execution of production and process control functions and documented at the time of performance.

Specifically, your firm has not set critical parameters for defect action limits, including but not limited to defects such as particulate matter, found within the drug product. The following batches were released without an understanding of the defects present, more specifically, particulate matter of unknown origin and composition at the time of release:

- (b) (4) which had 224 plugs rejected due to an unknown particulate matter,
  (b) (4) which had 45 plugs rejected due to unknown particulate matter,
  (b) (4) which had 37 plugs rejected due to unknown particulate matter – all three lots were released for intended commercial use on 12JAN2017 without critical defect limits established.
- Lots (b) (4) [redacted] were released for human use in Clinical Trials [redacted] respectively; without identification of critical defects and without critical defect limits established.

OBSERVATION 3

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

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Specifically, your firm lacks documentation to show that your product can consistently meet specifications as you have not systemically evaluated the (b) lots manufactured from FEB2016 to present, of which (b) failed specification and were disposed of in-process, and (were used for development purposes or training, (b were released for commercial use and (are pending release.

OBSERVATION 4

The responsibilities and procedures applicable to the quality control unit are not in writing.

Specifically,

A. Your QCU does not issue all batch records to manufacturing. Per SOP-10045, Work Order Request, Rev.002 and SOP-10064, Special Work Order Request, Operations is responsible for "printing all required documentation to complete the manufacturing process i.e. batch records, forms..." Additionally, the QCU does not have oversight of the manufacture of Engineering Builds, as these batches do not require the assignment of a lot number by the Document Control Coordinator. Since February of 2015, [redacted] manufacturing records were issued by Operations; [redacted] lots are marked as released for commercial use, (b lots are pending release for commercial use, the remaining (b lots are marked as development lots. Your QCU does not have the proper oversight for batch initiation and execution of GMP batches.

B. Additionally, you have not defined the responsibilities of your Quality Inspectors and Quality Engineers (e.g QA/QC).

C. Dextenza (Dexamethasone Punctum Plug 0.4mg) Lots (b) (4) [redacted] (originally intended for Clinical Use) and Lot (b) (4) [redacted] (originally intended as a Stability Lot), were discarded on 19SEP2016 without appropriate approval from Quality, without justification and without supporting disposition documentation. Products disposal procedures and documentation requirements are not adequately captured in SOP-10129 Handling and Storage, Rev. 003.

OBSERVATION 5

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Laboratory controls do not include the establishment of scientifically sound and appropriate specifications and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically,

A. Your firm failed to show that your test methods for Dextenza (Dexamethasone Punctum Plug 0.4 mg) are stability indicating, e.g. validation studies do not include forced degradation studies of your finished drug product or an analysis of peak purity.

B. The analytical balance used to weigh standards used in analyses related to your drug product Dextenza (Dexamethasone Punctum Plug 0.4mg) has not been appropriately qualified for use. Additionally, the [redacted] external weight checks performed do not encompass the full range of materials weighed. For example: [redacted] of Dexamethasone USP standard is weighed for the product release analysis: [redacted] of Dexamethasone Punctum Plugs on the analytical balance (b) (4) [redacted] but the [redacted] external check is performed [redacted] weights.

OBSERVATION 6

Employees engaged in the manufacture, processing, packing and holding of a drug product lack the training required to perform their assigned functions.

Specifically,

A. Your firm's training procedures for the (b) (4) inspection of Dextenza (Dexamethasone Punctum Plug 0.4mg) drug product are deficient with respect to effectiveness checks and on-going job specific re-training. Your firm has not established appropriate procedural controls that ensure robustness of identification techniques for defects observed in your drug product through training and documentation of training. Technicians responsible for identifying defects rely on verbal managerial training and a visual defect classification reference sheet. No defect library is presented and no assessment of the technician's ability to appropriately identify critical defects, such as particulates, is performed.

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B. Additionally, Dextenza (Dexamethasone Punctum Plug 0.4mg) Lots (b) (4) ; (b) (4) were released for human use in Clinical Trials on and , respectively, were processed without visual training aids to identify critical defects such as particulate matter.

***DATES OF INSPECTION**
4/24/2017(Mon),4/25/2017(Tue),4/26/2017(Wed),4/27/2017(Thu),4/28/2017(Fri),5/04/2017(Thu)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."