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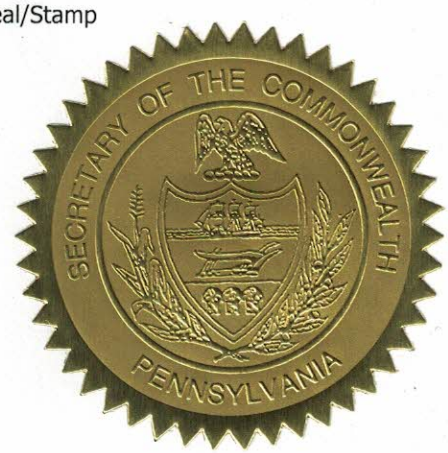
3. acting in the capacity of NOTARY PUBLIC
4. bears the seal/stamp JOSEPH A BUCKLEY , NOTARY PUBLIC, BUCKS COUNTY, COMMONWEALTH OF PENNSYLVANIA

Certified

5. at Harrisburg, Pennsylvania
6. The 25th day of August, 2020
7. by Kathy Boockvar, Secretary of the Commonwealth of Pennsylvania
8. No: 202015517
9. Seal/Stamp



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Kathy Boockvar

Kathy Boockvar

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U.S. FOOD & DRUG ADMINISTRATION

Officer of Pharmaceutical Quality
Operations, Division II
4040 N Central Expressway, Suite 300
DALLAS, TX 75204
214-253-5200

11/02/2018

Alcon Research Laboratories Ltd.
6201 South Fwy, Aspex Facility
Fort Worth, TX, 76134-2099 US

Reference: Inspection Date(s):09/19/2018 - 09/24/2018
Location: Alcon Research Laboratories Ltd.
6201 South Fwy
Aspex Facility
Fort Worth, TX 76134-2099, US

Dear Scott A. Johnson:

We are enclosing a copy of the establishment inspection report (EIR) for the inspection that the U.S. Food and Drug Administration (FDA) conducted at your premises on the referenced locale and date(s). When the Agency concludes that an inspection is "closed" under 21 CFR 20.64(d)(3), it will release a copy of the EIR to the inspected establishment. This procedure is applicable to EIRs for inspections completed on or after April 1, 1997.

The Agency continually works to make its regulatory process and activities more transparent to the regulated industry. Releasing this EIR to you is part of this effort. The copy being provided to you comprises the narrative portion of the report; it may reflect redactions made by the Agency in accordance with the Freedom of Information Act (FOIA) and 21 CFR Part 20. This, however, does not preclude you from requesting additional information under FOIA.

If you have any questions regarding this letter, you may contact Charles D Brown via telephone at 214-253-5245 or email at Charles.Brown@FDA.HHS.GOV.

For more information on the U.S. FDA, please visit our website at www.fda.gov.

Sincerely,
Charles D. Brown -S

Digitally signed by Charles D. Brown -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300037490, cn=Charles D. Brown -S
Date: 2018.11.02 09:30:08 -05'00'

Charles D Brown
SUPERVISORY CONSUMER
SAFETY OFFICER
PHARMACEUTICAL QUALITY
INVESTIGATION BRANCH

FEI:1610287
Enclosure: Establishment Inspection Report (EIR)

Oficial de Calidad Farmaceutical
Operaciones, División II
4040 N Central Expressway, Suite 300
DALLAS, TX 75204
214-253-5200

11/02/2018

Alcon Research Laboratories Ltd.

6201 South Fwy, Aspex Facility

Fort Worth, TX, 76134-2099 US

Referencia: Fecha(s) de Inspección: 19/09/2018 – 24/09/2018

Ubicación: Alcon Research Laboratories Ltd
6201 South Fwy
Aspex Facility
Fort Worth, TX 76134-2099, US

Estimado Scott A. Johnson:

Estamos adjuntando una copia del Reporte de Inspección del Establecimiento (EIR) para la inspección de la Administración de Alimentos y Medicamentos (FDA) de Estados Unidos realizará en su establecimiento en el lugar y fecha referenciados. Cuando la Agencia concluye que una inspección está "cerrada" bajo el 21 CFR 20.64(d)(3), liberará una copia del EIR al establecimiento inspeccionado. Este procedimiento es aplicable a los EIRs para inspecciones completadas el o después de 01 de Abril de 1997.

La Agencia continuamente trabaja para hacer sus procesos regulatorios y actividades más transparentes a la industria regulada. Liberando este EIR a usted como parte de este esfuerzo. La copia que se le proporciona comprende la parte narrativa del informe; puede reflejar redacciones hechas por la Agencia de acuerdo con el Acto de Libertad de Información (FOIA) y el 21 CFR Parte 20. Esto, sin embargo, no lo imposibilita a solicitar información adicional bajo el FOIA.

Si tiene alguna pregunta respecto a esta carta, puede contactar a Charles D Brown vía telefónica al 214-253-5245 o vía email a Charles.Brown@FDA.HHS.GOV

Para más información sobre la US FDA, por favor visite nuestro sitio web www.fda.gov

Sinceramente,
[Firma Digital]
Charles D Brown
SUPERVISOR DEL CONSUMIDOR
OFICIAL DE SEGURIDAD
CALIDAD FARMACÉUTICA
SUCURSAL DE INVESTIGACIÓN

FEI: 1610287
Carta adjunta: Reporte de Inspección del Establecimiento (EIR)

Administración de alimentos y medicamentos de los Estados Unidos (U.S FDA)
www.fda.gov

Declaro que esta traducción es copia fiel a la original

Garin Hoyng Bernardita

Digitally signed by Garin Hoyng Bernardita
DN: dc=com, dc=novartis, ou=people, ou=GD, serialNumber=871698, cn=Garin Hoyng Bernardita
Date: 2020.09.25 11:55:16 -03'00'

Bernardita Garin H.
Director Técnico
Novartis Chile S.A

Drug Establishments Current Registration Site

New Search

Search Results for **Alcon Research LLC**

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Firm Name	FDA Establishment Identifier	DUNS	Business Operations	Address	Expiration Date
Alcon Research LLC	1610287	007672236	MANUFACTURE;	6201 South Freeway, Fort Worth, Texas (TX) 76134, United States (USA)	12/31/2020

Showing 1 to 1 of 1 entries

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Data Current through: Thursday, Sep 24, 2020

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Establishment Inspection Report	FEI:	**1610287**
Alcon Research Laboratories Ltd.	EI Start:	9/19/2018
Fort Worth, TX 76134-2099	EI End:	09/24/2018

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SUMMARY

This Post Approval Inspection for the Manufacturer of [redacted] used to treat glaucoma and to control eye pressure was requested by the Office of Pharmaceutical Quality Operations Division II, FY18 Human Drug Post Approval Inspection under MARCS OP ID #63853. The inspection was conducted in accordance with CPGM 7346.843 Post Approval Audit Inspections and CPGM 7356.002 Drug Manufacturing Inspections. Follow up to Consumer Complaint #151390 was conducted. PAC codes covered this inspection were 56002, 56843 and 46R801.

The previous inspection conducted by the FDA occurred on 7/24/2017 through 8/4/2017 and resulted in the issuance of a two item FDA483, Inspectional Observations regarding procedures designed to prevent microbiological contamination of drug product purporting to be sterile are not established, written and followed and laboratory controls do not include the establishment of scientifically sound and appropriate specifications designed to assure that the drug product conform to appropriate standards of identity, strength, quality and purity. The inspection was classified VAI. Firms response to the observation issues with corrective actions and preventative actions appear to be adequate.

This inspection focused on the firm's product [redacted] Pre-Approval Inspection for this product was waived and the product that has been in distribution since April 2013. In addition, a follow up to

consumer complaint regarding an adverse reaction to [redacted] eye drops was conducted. The following systems were covered during this inspection: Quality, Material, Facilities & Equipment, Production, Laboratory and Packaging & Labeling. Process Validation Records, Cleaning Validation Records, Complaints, Training Files, Deviations Reports, Annual Product Reviews and Stability Records were some of the documents that were reviewed during this inspection. The firm is registered with the FDA.

No significant deficiencies were noted upon conclusion of this inspection, therefore, no FDA483, Inspectional Observations were issued at closeout. I stated that the firm appears to be in a state of control. The importance of packaging employees following their written procedures was discussed at closeout. I stated that this was not an all-inclusive inspection and upon further review, the conditions listed in the report may be considered violations of the FDC Act or other legal statues. I stated that it is their responsibility to ensure that they adhere to all the regulations that pertain to me. Legal sanctions available to FDA include issuance of a warning letter, seizure, injunction, civil money penalties and legal prosecution.

ADMINISTRATIVE DATA

Inspected firm:	Alcon Research Laboratories Ltd.
Location:	6201 South Fwy, ASPEX Facility Fort Worth, TX 76134-2099
Phone:	817-293-0450
FAX:	817-568-7170
Mailing address:	6201 South Fwy Fort Worth, TX 76134-2001
Email address:	www.alcon.com
Dates of inspection:	9/19/2018
Days in the facility:	4
Participants:	**Patty P Kaewussdangkul, Investigator**

On 09/19/2018, I presented my credentials and issued a "Form FDA 482, Notice of Inspection" (attached) to 'Scott A. Johnson, Site Quality Head-Alcon Sterile Product Expansion (ASPEX)' who stated that he was the most responsible person at time of my arrival. The following individuals were present when credentials were displayed:

- Patrick Collier, ASPEX Site General Manager
- Eileen Castro-Toro, ASPEX Head Quality Systems and Compliance
- Matt Callesen, ASPEX QA Operations Head
- Zachary Comiskey, ASPEX Head of Manufacturing
- Nick Holms, ASPEX Head of Engineering
- Helen Nestor, ASPEX Head of Materials
- Keith Nelson, ASPEX OpEx Head
- Don Kirkland, Alcon Quality Director, Compliance
- Dale Schaper, FWN (Fort Worth North) Quality Director, Compliance, QA GXP Compliance

- Aaron Holms, FWN QA Operations Head
- Victor Perez, FWN Head of Quality Systems & Compliance
- Ryan Blair, ASPEX Senior Analyst, Regulatory Compliance

See Exhibit 1 for Firm's Organization Charts.

All post inspectional correspondence should be addressed to:
Mr. Scott A. Johnson, Site Quality Head-Alcon Sterile Product Expansion
Alcon Research Laboratories Ltd.
6201 South Fwy, ASPEX Facility
Fort Worth, TX 76134-2099

HISTORY
Alcon was established in 1945 by founders Robert Alexander and William Conner. The name Alcon was formed by a combination of letters in the founder's last names. In 1978, Alcon was acquired by Nestle S.A. At time of inspection, Alcon Research Laboratories, Ltd is a subsidiary of Novartis Pharmaceuticals Corporation. The firm is a manufacturer of drugs and medical devices.

There are two sites at Alcon Research Laboratories: Fort Worth North (FWN) and Alcon Sterile Product Expansion (ASPEX). The sites are located across the street from one another and are registered with the FDA under one FEI number. The last GMP inspection of the facility which covered both FWN and ASPEX was conducted on July 24, 2017 through August 4, 2017 which resulted in two FDA483s, Inspectional Observations. Firm's response to the observations were reviewed and FMD letter was issued. See Exhibit 2 for FMD letter to previous FDA inspection.

The firm business hours are Monday through Friday, 8am to 5pm.
The firm production hours are 24 hours, 7 days a week which occurs in 4 shifts.

The firm stated that there are roughly 600 employees of which 99 are dedicated to Quality Assurance (QA). The firm's global headquarters is in Geneva, Switzerland.

INTERSTATE (I.S.) COMMERCE
The scope of this inspection is to cover the production of [redacted], a drug used to treat glaucoma and interocular pressure that is manufactured onsite at ASPEX. The firm distributes [redacted] finished product to a distribution center located in Pennsylvania where it is then distributed to customers.

See Exhibit 3 for Bill of Lading Document #81017441 dated 07/25/2018 showing [redacted] Lot #301280F shipped to Novartis Pharmaceuticals Corp,. located at 300 Salem Church Rd in Mechanicsburg PA 17050.

See Exhibit 4 for Bill of Lading Document #81018174 showing [redacted] Lot #294400F shipped to Novartis Pharmaceuticals Corp,. located at 300 Salem Church Rd in Mechanicsburg PA 17050.

See Exhibit 5 for Bill of Lading Document #81024033 showing [redacted] Lot #297667F shipped to Novartis Pharmaceuticals Corp,. located at 300 Salem Church Rd in Mechanicsburg PA 17050.

JURISDICTION (PRODUCTS MANUFACTURED AND/OR DISTRIBUTED)

The firm is a Manufacturer of Medical Devices and Sterile Ophthalmic Drugs that are distributed within the Unites States and abroad. The product [redacted] is distributed within the United States and overseas. Since 2016, a total of 61 lots consisting of [redacted] has been manufactured for the US market, See Exhibit 6.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

Below is the list of employees that I interacted with during the audit:

Function	SME	Title
Site Head	Scott Johnson	QA Site Head
QA Compliance	Eileen Castro- Toro	Head Quality Systems and Compliance
	Ryan Blair	Senior Analyst – Regulatory Compliance
QA Technical Support:	Rachael Armistead	Technical Support Specialist II
	Alan Villa	Sr. Technical Support Specialist
	Michael Bosman	Technical Support Specialist
Analytical Science & Technology	John Shaw	Product Steward
	Rushmila Hossain	Principal Validation Engineer
Materials	Martin Sedtal	Senior Buyer
Compounding	Chris Japak	Sr. Manager Production
	Richard Triggs	Production Supervisor
Filling	Aditya Basrur	Production Supervisor
	Kerry Poehlein	Production Lead
Packaging	Chuck Walton	Production Manager
Microbiology	Ricky Nguyen	Sr. QA Analyst
	Dwayne Favors	Principal Analyst
Chemistry	Ben Lewis	Laboratory Manager
	Joleen Faucette	Sr. QA Analysist I
Engineering	Steven Medina	Critical Systems Manager
	Bruce Davis	Maintenance Technician – Critical Utilities
Quality Assurance	Matt Callesen	QA Operations Head
	Ashley Hsieh	QA Process Engineer
	Darin Wedel	Sr. Engineer I
Medical Safety (Basel & NJ) Conference Call	Meghan Graham	Manager Vigilance Process Assurance
	Stacy Spring	Head of CMO & PS QA
	Tony DeSousa	US Count Patient Safety Head
	Sheila Bell	US Head of PV Operations
	Debra Wolff,	Global Head CMO & PS QA
	Maryann Karolchyk	Global Head of Safety Science
	Howard Snow	Head PS Ophthalmology

	Cynthia Green	US Complaint & Management Lead
	Mike Mejia	Sr. QA Analyst I/ QA Operations
QAMI	Tim White	Supervisor
FWN Tour (Warehouse, Incubators, QA Rooms, Raw Material Lab, Sterility Lab)	Victor Perez	Head of Quality Systems & Compliance
	Aaron Holms	QA Operations Director
	Coy Mills	Quality Control & AS&T Director
	Ussma Quraishi	Process Support Lead
	Marcie Poston (Incubator QA Rooms)	QA Supervisor
	Jeremy Jacob (Raw Material Lab)	QA Supervisor
Raw Materials Warehouse	Eileen Castro- Toro	Head Quality Systems and Compliance
	Scott Johnson	QA Site Head
	Ussma Quraishi	Process Support Lead
	Victor Perez	Head of Quality Systems & Compliance
	Darin Wedel	Senior QA Engineer
	Tim White	QA Operations Supervisor
Chemistry Lab Tour	Ricky Nguyen	Sr. QA Analysist I
	Ben Lewis	Laboratory Manager
	Eileen Castro- Toro	Head Quality Systems and Compliance
	Nathan Raschke	AS&T Manager
	Matt Callesen	QA Operations Head
Compounding Tour	Eileen Castro- Toro	Head Quality Systems and Compliance
	Chris Japak	Sr. Manager Production
	Zach Comiskey	Manufacturing Site Head
	Matt Callesen	QA Operation Lead
Fill/Pack Tour	Aditya Basrur	Manufacturing Supervisor
	Chuck Walton	Production Manager
	Zach Comiskey	Manufacturing Site Head
	Matt Callesen	Head QA Operations
	Eileen Castro -Toro	Head Quality Systems and Compliance

I requested the Position Descriptions for the following firm employees:

- Scott A. Johnson, Quality Site Head ASPEX
- Zachary R. Comiskey, Manufacturing Head, ASPEX
- Charles Walton Jr., Manufacturing Production Manager
- Christopher Jon Japak, Senior Manager of Production
- Matthew L. Callesen, Quality Operations Lead-ASPEX
- Benjamin D. Lewis, QA Laboratory Manage

See Exhibit 7 for Corresponding Position Descriptions.

FIRM'S TRAINING PROGRAM

Mrs. Eileen Castro-Toro, ASPEX Head Quality Systems and Compliance is responsible for the firm's training program. She stated that all training is monitored in Plateau, a software learning system used to handle training for employees such as cGMP refresher training that is required on an annual basis as well as each employees' individual development as it pertains to their job duties and responsibilities. See Exhibit 8 for Firm's Plateau Report for Annual CGMP Refresher Training Module Trainee List. Mrs. Castro-Toro stated that each employee has their own unique user id and passcode for Plateau and the system notifies employees for training that needs to be completed as well as notifies Supervisors/Managers of those who have missed their deadlines. No deficiencies were seen upon review of the firm's training program.

MANUFACTURING/DESIGN OPERATIONS

QUALITY SYSTEM

The firm has a Quality System in place that has the duties and responsibilities to ensure that all raw materials, drug components, labeling and packaging meet specification prior to use. The Quality System ensures that all finished product meet specification prior to release for distribution to their customers. The firm's Quality System is responsible for ensuring that errors, deviations, non-conformances in manufacturing and test are investigated to determine a root cause. The Quality System is responsible for the implementation of corrective and preventative actions.

No deficiencies were seen upon review of the validation reports conducted for [redacted] The validation process included launch batches as well as batches placed on stability. There were no deviations to the manufacturing process and the firm is capable of consistently manufacturing this product.

No deficiencies were noted upon review of the past two annual product reviews for [redacted] which cover the following time periods: 01-April 2016 to 31-March 2017 and 01-April 2017 to 31 March 2018. The firm's reviews starting materials, product batches, deviations, change control, complaints and adverse trends are conducted.

The firm stated that they have Release Agents that are part of the firm's QA whose sole duty and responsibility is to release batches. The firm stated that the entire process is reviewed, from the raw material release records, components, change controls and that all laboratory data was reviewed by QC. Certificate of Analysis are provided to customer once product is released, See Exhibit 9 for Certificate of Analysis for [redacted] Finished Product.

MATERIAL SYSTEM

No deficiencies were seen upon review of how the firm handles receipt of raw materials, components, packaging, labeling and finished drug substances. All material is tested prior to release for use. Certificate of Analysis are maintained from the supplier of materials. See Exhibit 10 for Certificate of Analysis for [redacted] from Cedarsburg Pharmaceuticals located in

Wisconsin and Exhibit 11 for Certificate of Analysis for [redacted] rom Finorga located in France which are the two actives used in [redacted] See Exhibit 12 for Firm's Specifications for [redacted] and Corresponding COA and Exhibit 13 for Firm's Specifications for [redacted] nd Corresponding COA. The COA for the active pharmaceutical ingredients is the release for use.

Materials are selected implement the first in first out method to ensure proper rotation of materials received. All materials are placed in quarantine at receipt until release by QA. Release by the QA is dependent on testing for specification set for each material. Raw material and sterility tests are conducted at Fort Worth North. See Exhibit 14 for Component Testing List which lists the inventory of components on hand and quantities needed for testing. No deficiencies were seen upon review of the firm's supplier verification program.

The firm receives the eye dropper caps, bottles, and plugs sterile from their approved suppliers. The firm stated that these container components are either gamma sterilized or ETO sterilized.

According to the firm, there are some tests for raw material that are contracted to:
Quality Chemical Laboratories located at 3400 Enterprise Drive in Wilmington, NC 28405.
The firm also audit's their contract laboratories and no deficiencies were noted upon review of the report.

The firm manufactures Purified Water/WFI on the ASPEX, See Exhibit 15 for Firms' Purified Water/WFI Schematic at ASPEX. The ports are sampled on a rotational basis to ensure that testing is conducted on all ports of use. The ports of use that were in the Compounding Area that were seen during walkthrough were MV-1801, MV-1802, MV-1803. The firm stated that the water is tested for endotoxin daily and the ports of use are tested for total organic carbon and conductivity.

FACILITIES & EQUIPMENT

The ASPEX facility has seven compounding rooms, five filling lines identified as A through E and six packing/labeling lines. The firm is current with their clean room classifications. No deficiencies were noted upon review of Line E filling room classification. The filling area is classified as ISO5 surrounded by a ISO7 area. The firm conducts personnel monitoring, active and passive air sampling. Sterile garb is worn prior to entry of the filling room.

The firm has conducted cleaning validation studies to ensure that their cleaning process can prevent cross contamination as the equipment used in the production of [redacted] is not dedicated. The firm's approach to cleaning validation is to determine the worst-case product. No deficiencies were noted upon review of the firm's cleaning validation.

The firm has ample space to conduct their manufacturing activities. Compounding is conducted on the 2nd floor, Filling and Packaging are conducted on the 1st floor. The firm appears to be in a state of good repair. All equipment is clearly identified and is made of stainless steel. Equipment such as

balances and pH meters were within calibration. The firm has a calibration schedule to ensure that there are no lapses in calibration.

PRODUCTION SYSTEM

The firm stated that the production of [redacted] occurs in three phases: menstruum, vehicle and isolation. I was not able to observe the production of [redacted] as it was not on the production schedule at time of inspection. However, the manufacturing process of [redacted] was explained to me. See Exhibit 16 For [redacted] Process Flow Chart. The two active ingredients in [redacted] is [redacted] which are compounded separately and sterilized prior to mixing together and aseptically filled to form [redacted] the finished product. [redacted] cannot be filtered sterilized therefore undergoes autoclave sterilization. [redacted] is filter sterilized. See Exhibit 17 for [redacted] Formulation Sheet. Compounding of the product is conducted on the 2nd floor. See Exhibit 18 for Firm's Compounding Area Diagram.

The [redacted] is autoclaved and transfer of product is conducted in an isolator which is purged with hydrogen peroxide prior to opening product. The employee conducting the transfer does not go in the isolator rather there is body suit affixed to the isolator where an employee steps into and does the manipulations needed to transfer the slurry. The slurry is then mixed with the filter sterilized Brimonidine Tartrate and is ready to be aseptically filled on the 1st floor.

Compounding of [redacted] Lot #305041F was in process during walkthrough of compounding area.

The firm performs personnel monitoring and environmental (active and passive) monitoring during each aseptic fill. Employees must don sterile wear which includes hood, gown, boots and gloves prior to entry of fill area. The filling occurs in an enclosed area that is classified ISO5 and surrounding areas are classified ISO7. Filling is an automated process with ends with "white stock". The firm states that white stock are unlabeled finished drug products to be labeled later.

Filling of [redacted] Lot #297193F was observed on Line E. See Exhibit 19 for Firm's Filling Areas and Packaging Line. Line E may be used in the production of [redacted]

No deficiencies were seen upon review of the firm's production system. All significant steps are documented in a contemporaneous manner. Required elements such as but not limited to yield calculations, examples of labeling, label reconciliation, equipment identification numbers are within the batch production records. No deficiencies were observed upon review of [redacted] Batch Production Records.

LABORATORY

ASPEX site conducts all finished product testing for [redacted] except for the sterility test which is conducted across the street at Fort Worth North Laboratory. Refer to Exhibit 9 for Certificate of Analysis of [redacted] Lot #297669F which lists all the tests that are conducted on finished product

for release. There have been no sterility failures. Endotoxin testing for [redacted] and other eye drops are not required and the supplement to the [redacted] has been approved. No deficiencies were seen upon walkthrough of laboratory areas. Equipment that I observed in the laboratories were calibrated. User Ids and passwords are required to log into and run tests. Users have no delete capability and integrity of data is maintained.

The firm gives a 24-month expiration for [redacted] packaged in 5mL/8mL, 8mL/10mL and a 12-month expiration for [redacted] packaged in 2.5mL/4mL bottles. The firm has conducted stability studies to support the expiration dates given on the product. The firm also conducts ongoing stability studies and no issues were noted upon review of lots placed in stability. No deficiencies were seen upon review of stability data. Retain samples are kept for each lot of product and kept for one year after expiration date.

Media fills are conducted at least twice a year on each line. I requested the records of the last media fill conducted on Line E. The last media fill conducted on Line E was executed on February 23, 2018 and no deficiencies were observed. No less than 10,000 units are filled. Factors that contribute to worst case scenarios such as late shifts, fatigue employees, number of employees, duration of fill and bottles sizes are considered when conducting a media fill. Every batch of [redacted] is tested for sterility across the street at Fort Worth North. There were no sterility failures for the past two years.

PACKAGING & LABELING

Packaging of [redacted] Lot #295224F was observed during the audit and the firm stated that the packing and labeling process conducted for [redacted] would be the same. Packaging and labeling of [redacted] is conducted automatically. Unlabeled finished product bottles (white stock) are fed onto a cylinder that will feed onto a conveyor belt where principal label is affixed and 2D UV code is placed on the bottle. The secondary containers are assembled into boxes and package inserts are placed in the boxes along with the labeled finished products.

During visual audit of the packaging and labeling of [redacted] Lot #295224F, I observed empty assembled boxes falling onto the cartoner machine floor which is enclosed and not the designated reject bin. The firm stated that on occasion, the box may not have the package insert or may be missing a bottle which will be acknowledged by the machine and the machine will automatically reject these cartons into the designated reject bin. I asked the firm what happens to the boxes that fall onto the cartoner floor and the firm stated that they are rejected.

However, I observed the packaging employee remove the empty assembled boxes that did not go in the designated reject bin and placed them in a bin to be reclaimed. When I pointed this out to the firm the packaging employee removed the bin from the table. I asked the firm where she was taking the bin and was told that they were being rejected.

Upon reviewing the firm's SOP, it clearly states that any cartons that fall onto machine interior is to be rejected. Only cartons that fall into the clearly marked reject bin can be reclaimed (returned to the packaging process) once they are examined to be acceptable for use. I stated that the packaging

employee did not follow written procedures. Furthermore, I stated that according to the SOP, the boxes should have been rejected and not placed in the reclaim bin. The importance of packaging employees following their written procedures was discussed at closeout.

12 individual units of [redacted] Lot#295224 are plastic wrapped together as one set and 4 sets are placed in a cardboard shipping box. According to the firm, [redacted] is also packaged in the same fashion. See Exhibit 20 for [redacted] Lot #297669F Primary Label which is placed on the product container. See Exhibit 21 for [redacted] Package Insert and Exhibit 22 for Secondary Container Label.

MANUFACTURING CODES

[redacted] Lot #297667F, [redacted] Lot #294400F and [redacted] Lot #297667F. The firm stated that the number is generated by a system and there is no specific meaning to the numbers. However, the letter "F" indicates that it was manufactured in Fort Worth, Texas. I asked the firm for another example of where the letter changes and was told that lot codes ending in "S" means that they were produced in Singapore.

COMPLAINTS

Consumer Complaint #151390 was received by the FDA on October 30, 2017 on regarding an adverse reaction from the use of [redacted] which is used to treat eye infections. FDA conducted a follow up which included visits to the complainant and the physician, See Attachment 2 for CC #151390 Follow Up Memorandum. The complainant stated that use of the [redacted] resulted in an eye injury and infection. The complainant was administered a combination of [redacted] and [redacted] by her Physician at time of appointment and was given a prescription of [redacted] to administer herself for the next 30 days. The physician was contacted by FDA and he submitted a statement indicating that he did not believe that the [redacted] was the cause of the eye injuries, See Attachment 3 for Physician Statement. The Doctor diagnosed the patient with a corneal ulcer.

On 9/22/2018, There was a conference call with the Medical Safety Team which are based in Switzerland and New Jersey, refer to Individual Responsibility and Persons Interviewed Section to see participants. The firm was aware of this specific complaint and stated that upon review of the evidence, it appears to be an expected adverse reaction that users may experience. The firm provided a package insert of [redacted] which lists all expected adverse reactions, See Exhibit 23. Furthermore, they explained that all consumer complaints received by the team are triaged to determine adverse reactions vs. issues with manufacturing. The site of inspection may not be aware of any serious adverse reactions unless the Medical Safety Board assessed the complaint and requested an investigation to the manufacturing of the implicated product. The firm stated that they handle all manufacturing related complaints such as issues with fill volume, dispensing issues, leaking, and visual quality defects of the drug products.

A Field Alert Report was submitted to FDA electronically 6/13/2018 for an adjustment of the fill equipment that was damaging bottles. An investigation was conducted, a root cause determined and implementation of corrective actions to prevent similar issues was conducted for all filling lines. See Exhibit 30 for Firm's Field Alert Report.

The firm has several written procedures on how to investigate consumer complaints. There is a procedure for Alcon worldwide, See Exhibit 24. There is a written procedure for complaints that are handled in Fort Worth, Texas, See Exhibit 25. Alcon is a contract manufacturer for Novartis therefore, they have a complaint procedure that is specific to Novartis drug products, See Exhibit 26.

No deficiencies were noted upon review of their complaint log since April 2018 to time of inspection, See Exhibit 27. It appears that complaints are investigated thoroughly and within reasonable timeframes.

RECALL PROCEDURES

No recalls have been conducted for [redacted] for the past two years. The firm provided their written procedures for conducting recalls, See Exhibit 28. The firm stated that a mock recall is conducted on a yearly basis. The last mock recall was conducted in 2017.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

No significant observations were noted during this inspection therefore no FDA483, Inspectional Observations was issued at closeout.

REFUSALS

No refusals were encountered during this inspection.

GENERAL DISCUSSION WITH MANAGEMENT

On 9/24/2018, I held a closeout meeting with the following individuals:

- Scott A. Johnson, ASPEX Quality Site Head
- Patrick Collier, ASPEX Site General Manager
- Eileen Castro-Toro, ASPEX Head of Quality Systems and Compliance
- Zachary Comiskey, ASPEX Head of Manufacturing
- Nick Holms, ASPEX Head of Engineering
- Keith Nelson, ASPEX OpEx Head
- Ari Gordon, ASPEX HR Head
- P. J. Quevedo, Fort Worth North Manufacturing HR Head
- Ryan Blair, ASPEX Senior Analyst- Regulatory Compliance

I stated that the firm appears to be in a state of control. I stated that no significant observations were observed during the audit therefore no FDA483, Inspectional Observations was issued. However, I reminded that the firm needs to ensure that their packaging employees follow written procedures was discussed at closeout. I observed an employee placed empty cartons that were to be rejected according to their standard operating procedures placed into the rework bin. Refer to Packaging and Labeling under Manufacturing/Design Operations section. The firm provided a response to this verbal discussion item, See Exhibit 29.

No deficiencies were noted upon firm's handling of the consumer complaint #151390 received by FDA in October 2017. The team responsible for handling adverse reactions did investigate this specific complaint and it was determined to be a known adverse reaction. Furthermore, the complainant doctor stated that it was his professional opinion that the drug was not the cause of the symptoms that the patient was experiencing.

I stated that this is not an all-inclusive inspection. Upon further review by the agency the conditions listed in the report may be considered violations of the FDC Act or other legal statues. I told the firm that it is their responsibility to ensure that they adhere to all applicable rules and regulations as it pertains to their business. Sanctions available to the FDA include issuance of a warning letter, seizure, injunction, civil money penalties and legal prosecution.

I provided a copy of ORA Program Alignment Information Sheet to Mr. Patrick Collier, ASPEX Quality Site Head and asked if the firm had any questions before ending the inspection.

ADDITIONAL INFORMATION

The firm stated that Novartis Pharmaceuticals Corp will be leaving Fort Worth, TX in 2019.

SAMPLES COLLECTED

No samples were collected during this inspection.

VOLUNTARY CORRECTIONS

The firm appears to have corrected the two inspectional observations issued last inspection which was conducted from 7/24/2017 to 8/4/2017.

EXHIBITS COLLECTED

1. Firm's Organization Charts. (2pgs)
2. FMD Letter
3. Bill of Lading Document #81017441. (2pgs)
4. Bill of Lading Document #81018174. (2pgs)
5. Bill of Lading Document #81024033. (2pgs)
6. [redacted] Lots Manufactured since 2016.

7. Position Descriptions. (17pgs)
8. Annual CGMP Refresher Training Attendee List. (22pgs)
9. Certificate of Analysis for Finished Lots of [redacted] (2pgs)
10. Supplier Certificate of Analysis for [redacted]
11. Supplier Certificate of Analysis for [redacted] (3pgs)
12. Firm's Specifications for [redacted] and Certificate of Analysis Release. (2pgs)
13. Firm's Specifications for [redacted] and Certificate of Analysis Release. (3pgs)
14. Raw Component Testing List. (8pgs)
15. Firms' Purified Water/WFI Schematic. (2pgs)
16. [redacted] Process Flow Chart
17. [redacted] Formulation Sheet.
18. Firm's Compounding Area Diagram.
19. Firm's Filling Areas and Packaging Line Diagram.
20. [redacted] Lot #297669F Primary Label.
21. [redacted] Package Insert. (2pgs)
22. [redacted] Secondary Container Label.
23. [redacted] Package Insert.
24. Alcon Global Consumer Complaint Procedures. (34pgs)
25. Alcon Site Consumer Complaint Procedures. (9pgs)
26. Novartis Consumer Complaint Procedures. (31pgs)
27. Site Complaint Log since April 2018.
28. Firm's Recall SOP. (28pgs)
29. Firm's Response to Discussion Item. (2pgs)
30. Firm's Field Alert Report. (4pgs)

ATTACHMENTS

1. FDA482, Notice of Inspection (3pgs)
2. FDA Memorandum for Consumer Complaint #151390. (2pgs)
3. Physician Statement for Consumer Complaint #151390.

Patty P. Kaewussdangkul -S

Digitally signed by Patty P. Kaewussdangkul -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300178629, cn=Patty P. Kaewussdangkul -S
Date: 2018.10.28 14:51:05 -05'00'

Certified to be a TRUE COPY on this 18th day of August, 2020, Joseph A Buckley, Notary Public

COMMONWEALTH OF PENNSYLVANIA
NOTARY SEAL
JOSEPH A BUCKLEY, Notary Public
Borough of Morrisville, Bucks County
My Commission Expires: Oct. 15, 2022
Commission Number 1227727

Joseph A Buckley
Pennsylvania Notary Public
CERTIFIED TRUE COPY