December 15, 2023

EYE DROP SAFETY ALERT:
Adverse Manufacturer Inspection Results

Regenerative Processing Plant LLC, manufacturer of Regener-Eyes LITE and Regener-Eyes PRO

In June 2023, the FDA conducted its first inspection of Regenerative Processing Plant LLC's drug manufacturing facility in Palm Harbor, Florida. In December 2023, a summary of the results was posted on the FDA's Data Dashboard. Due to the significant number of objectionable conditions and practices identified by the inspectors, the FDA applied the worst overall outcome of Official Action Indicated.

Dry Eye Foundation obtained a copy of the complete inspection report, called a Form 483, through a Freedom of Information Act request. Many of the violations cited in this report and on the FDA's Data Dashboard resemble those listed in the Form 483s of two other OTC ophthalmic manufacturers whose first-time drug facility inspections in 2023 resulted in product recalls: Global Pharma Healthcare Private Limited (manufacturer of EzriCare Artificial Tears, recalled in February) and Kilitch Healthcare India Limited (manufacturer of a large number of generic OTC eye drops, recalled in November.)

Regener-Eyes LITE and Regener-Eyes PRO continue to be recommended and sometimes sold to dry eye patients by their eye care providers. Therefore, as a matter of public safety, we are bringing the results of the FDA inspection to the attention of the Dry Eye Disease patient and provider communities.

Lack of competence in sterile ophthalmic manufacturing processes

The findings in Form 483 (attached), both in scope and nature, indicate that Regenerative Processing Plant LLC has failed to:

- properly construct and maintain cleanrooms
- maintain detailed records as required by law
- establish that its manufacturing processes are aseptic (sterile)
- fully investigate abnormal test results that demonstrated bacterial contamination of equipment
- confirm the purity of raw ingredients

15 regulatory law violations

According to the FDA's Data Dashboard, the Regenerative Processing Plant inspection resulted in citations for violation of 15 Federal regulatory laws. See Appendix 1 for details.

Extensive testing and quality control omissions and failures

Form 483 documents extensive failure to ensure aseptic and accurate manufacturing via process monitoring through the required battery of standard tests. These failures include: tests that were not conducted at all; tests that were improperly conducted; tests that were conducted with unvalidated processes; tests whose results were not documented; tests whose results were ignored; tests whose failed results were not fully investigated; and tests that were prematurely discontinued.

Five “critical deficiencies” were identified in Form 483 regarding quality control. The investigators stated that the list was “not all-inclusive”. (Observation 11)

Batches sold despite evidence of equipment contamination

A critical test that ensures that the entire manufacturing process does not introduce contamination is the *media fill.* In a media fill, a liquid called *media* that promotes the growth of bacteria and other microorganisms is run through all the equipment used in eye drop manufacturing in the same sequence that the raw ingredients would run through it. If there is any bacterial contamination on the equipment, it will wash off into the media. The media is stored under appropriate conditions to stimulate the growth of microorganisms and is tested periodically. If bacteria or fungal growth is identified, the manufacturer must perform a root cause analysis to determine which piece of equipment was at fault, comprehensively sterilize that device and all downstream equipment, and then repeat the media fill to establish that the machinery has been adequately sanitized and the entire manufacturing process is *aseptic* (does not introduce microorganisms into the finished product).

Form 483 states that batches of Regener-Eyes PRO and Regener-Eyes LITE that were manufactured both before and after failed or invalidated media fills were released for commercial distribution. (Observations 1, 11)

Batches sold despite evidence of inaccurate formulation

Form 483 states that 27% of all manufactured batches had a pH out of range, with readings from 7.7 to as high as 8.3. Nonetheless, these units were released for commercial distribution. In addition, units from batches whose glycerin content tested out of range were released for commercial distribution. (Observation 2)

Building, cleanrooms and environmental controls significantly substandard

Observations 5 and 7 document extensive deficiencies in the design, construction and maintenance of the cleanrooms. These include walls and ceiling of unsuitable construction; lack of written procedures for sanitizing surfaces; lack of validation that the cleaning processes in use are actually effective; and lack of proper air monitoring for particulates and pathogens.

In one cleanroom, inspectors observed that slats had been cut into the lower part of one wall to simulate the unidirectional air flow required in a cleanroom. These slats opened into an unmonitored area outside the cleanroom, allowing the influx of particulate-laden air into the cleanroom.

Room temperature storage and 24-month shelf life not justified

Regener-Eyes' stated storage temperature (room temperature) and shelf life (24 months) are not supported by Regenerative Processing Plant's own stability testing data. (Observation 3)

Product packaging not designed to prevent contamination

Regener-Eyes LITE and Regener-Eyes PRO are packaged in a bottle which is "not for single use nor does it have a backflow prevention design to prevent microbial contamination of the product after being shipped." (Observation 4)

Continued uncertainty about current and past ingredients in Regener-Eyes LITE and Regener-Eyes PRO

In Observation 9, investigators state that Regenerative Processing Plant reported to the FDA that Regener-Eyes LITE and Regener-Eyes PRO containing amniotic fluid were discontinued in June 2021.

See Appendix 2 for three different ingredient lists declared by Regenerative Processing Plant in its official drug listings for Regener-Eyes LITE and Regener-Eyes PRO in the past two years.

Records and samples of amniotic fluid eye drops missing

No bottles of amniotic fluid eye drops were retained as required by law, and no records related to these products could be located. The Chief Strategist stated that she "could not locate any records such as complaint records, distribution records, receiving records, storage records, and manufacturing records" and that she "could not remember where the records went or if they were destroyed or not". (Observations 9, 11, 14)

Concluding notes from Dry Eye Foundation

Based on FDA's inspection findings, it is clear that there is no assurance that Regener-Eyes PRO and Regener-Eyes LITE are manufactured in a correctly formulated and sterile fashion. We therefore urge the Dry Eye Disease community to avoid Regener-Eyes eye drops and we urge providers to stop recommending them.

Sincerely,

Sandra Brown MD (Medical Advisor)
Rebecca Petris (Co-Executive Director)
Aidan Moore (Co-Executive Director)

Appendix 1: Regenerative Processing Plant, LLC FEI 3011320041, Inspection 6/30/2023, Inspection Citation Details

Act/CFR Number	Short Description	Long Description
21 CFR 211.22(d)	Procedures not in writing, fully followed	The responsibilities and procedures applicable to the quality control unit are not fully followed.
21 CFR 211.42(a)	Buildings of Suitable Size, Construction, Location	Buildings used in the manufacture, processing, packing, or holding of a drug product do not have the suitable (sic) to facilitate cleaning, maintenance, and proper operations.
21 CFR 211.42(c)(10)(iv)	Environmental Monitoring System	Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.
21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not maintained at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.
21 CFR 211.67(b)	Written procedures not established/followed	Written procedures are not established for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.
21 CFR 211.84(d)(2)	Component identification test	Specific identification tests are not conducted on components that have been accepted based on the supplier's report of analysis.
21 CFR 211.94(b)	Protection from external factors	Container closure systems do not provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.
21 CFR 211.113(b)	Validation lacking for sterile drug products	Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include validation of the process.
21 CFR 211.160(b)(1)	Samples (various types) representative, identified properly	Samples taken to determine conformance to appropriate written specifications for the acceptance of each lot within each shipment of drug product containers are not representative.
21 CFR 211.166(a)	Results not used for expiration dates, storage cond.	Results of stability testing are not used in determining appropriate storage conditions and expiration dates.
21 CFR 211.170(b)(1)	Retention time of reserve samples, in general	You did not retain reserve samples for drug products for one year after the expiration dates of the drug products.
21 CFR 211.180(b)	Record maintenance 1 year (except exempt OTC)	All records of production associated with a batch of drug product were not maintained at least one (1) year after the expiration date.

21 CFR 211.188(b)(3)	Identification of each component or in-process material	Batch production and control records do not include the specific identification of each batch of component used for each batch of drug product produced.
21 CFR 211.192	Investigations of discrepancies, failures	There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.
21 CFR 211.194(a)(4)	Complete Test Data	Laboratory records are deficient in that they do not include a complete record of all data obtained during testing.

Appendix 2: Ingredient Lists for Regener-Eyes LITE and Regener-Eyes PRO

NDC (Regener-Eyes LITE)	NDC (Regener-Eyes PRO)	Active ingredient	Inactive ingredients
82305-002	82305-001	Glycerin	d-MAPPS™* and 0.9% Sodium Chloride USP
82305-006	82305-003	Glycerin	Tonicity Solution™** and sterile water
82305-006-01	82305-003-01	Glycerin	Sterile Water, Tonicity Solution Sodium Chloride***

** This ingredient has no Unique Ingredient Identifier; it appears on product packaging but not on the formal drug label; it is identifiable in medical literature and patent applications as amniotic fluid.*
*** This ingredient has no Unique Ingredient Identifier; it appears on product packaging but not on the formal drug label; it remains an unknown substance.*
**** We consulted the FDA's Office of Drug Information for information about this ingredient and they stated that it was simply the company's proprietary name for sodium chloride (salt). We have requested an unredacted version of Form 483 in order to verify this, due in part to the interaction between FDA and Regenerative Processing Plant described in Form 483's Observation 15.*

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Dr. Carl R. Harrell, Medical Director

FIRM NAME	STREET ADDRESS
Regenerative Processing Plant, LLC	34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Palm Harbor, FL 34684-2144	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 WE OBSERVED:
Since commencing manufacturing operations for both Regener-Eyes PRO and Regener- Eyes LITE ophthalmic eye drops (with glycerin) on 12/01/2021, your firm has manufactured and distributed (b) (4) bottles of Regener-Eyes LITE and (b) (4) bottles of Regener-Eyes PRO nationwide.

OBSERVATION 1
Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include validation of the process.

Specifically, your firm did not validate the manufacturing process for both your firm's Regener-Eys PRO and Regener-Eyes LITE ophthalmic solution eye drops (3ml) labeled for treating dry eyes (human) and purported to be sterile.

Since commencing manufacturing operations for Regener-Eyes PRO and Regener-Eyes LITE on 12/01/2021, you have attempted to conduct (b) (4) media fill studies (b) (4) each consisting of (b) (4) runs to validate your aseptic manufacturing process. (b) (4) studies were observed to not be valid for the following critical deficiencies (this list is not all inclusive):

a) Out of the (b) (4) runs conducted within the (b) (4) study from (b) (4) (b) (4) of the (b) (4) runs failed, with microbial contamination observed within run PRO (b) (4) and within run LITE (b) (4) . No investigations were conducted to determine the source of the contamination nor to determine potential impact to (b) (4) manufactured lots ((b) (4) LITE and (b) (4) PRO) prior to the media

AMENDMENT 1

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Travis S Bradley, Investigator Samantha J Pinizzotto, Investigator Ivan E Reyes, Investigator	X Travis S Bradley Investigator Signed By: Travis S. Bradley -S Date Signed: 06-30-2023 10:29:06	6/30/2023

fills. Additionally, you did not attempt to identify the species of microorganisms identified within all contaminated bottles.

b) Within the most recent study conducted from (b) (4) you did not incubate and examine all filled bottles of media for microbial contamination during each run. The following was observed:

- PRO (b) (4) - (b) (4) bottles filled (14%) were incubated and examined.
- PRO (b) (4) - (b) (4) bottles filled (12%) were incubated and examined.
- LITE (b) (4) - (b) (4) bottles filled (13%) were incubated and examined.

On 06/28/2023, while observing your in-process product storage area, it was observed that all non-incubated containers pertaining to media fill LITE (b) (4) were bagged and stored within a laboratory refrigerator with no justification for why the containers were being stored.

c) Out of the (b) (4) runs conducted within the media fill study from 11/16/2022 - 04/26/2023, (b) (4) runs (LITE (b) (4)) was invalidated due to a (b) (4) issue pertaining to a (b) (4) . (b) (4) commercial batches ((b) (4) LITE and (b) (4) PRO) were manufactured after the previous invalidated run. This study did not consist of (b) (4) successful runs.

d) Growth promotion testing was not conducted for the (b) (4) utilized to fill bottles in both media fill studies.

Since 12/01/2021, your firm has manufactured and distributed (b) (4) bottles of Regener-Eyes LITE and (b) (4) bottles of Regener-Eyes PRO.

AMENDMENT 1

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

OBSERVATION 2

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

a) Your defined pH range for Regener-Eyes PRO and Regener-Eyes LITE are identified as (b) (4) (b) (4) While observing analytical testing records for manufactured batches of both products, pH readings from 7.7 to as high as 8.3 were routinely observed. In total, a combined (b) (4) lots of both products ((b) (4) LITE and (b) (4) PRO) out of a total of (b) (4) total batches manufactured were found to have pH values greater than your high defined pH range of (b) (4) This equates to 27% of your total combined lots of Regener-Eyes PRO and Regener Eyes LITE being out of your defined range since you began manufacturing Regener-Eyes glycerin-based products ((b) (4) total batches manufactured). There is no documentation that these (b) (4) lots that were outside your specified pH range were investigated. Units were released for commercial distribution from these lots.

b) OOSs in process validation batches (PRO 120221, 120621, 120821, and LITE 120121, 120321, 120721) were observed for glycerin content at the (b) (4) stability timepoint through the (b) (4) stability timepoints as follows:

PRO (*glycerin specification:* (b) (4)

Lot	(b) (4)
120221	
120621	
120821	

AMENDMENT 1

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

LITE (*glycerin specification:* (b) (4)

Lot
120121
120321
120721

(b) (4)

In response to the OOS results, your investigation claimed the root cause to be laboratory error, but your contract laboratory's investigation does not support this as no error was identified. Additionally, you utilized a secondary laboratory after receiving the OOS results to continue the stability study but did not conduct a technical method transfer from your initial analytical laboratory to your secondary laboratory where you received in-specification results for samples later tested. Units from these OOSs stability batches were released for commercial distribution.

OBSERVATION 3

Results of stability testing are not used in determining appropriate storage conditions and expiration dates.

Specifically, your stability studies for Regener-Eyes PRO ophthalmic solution eye drops (3ml) do not support storage of the product at room temperature for 24 months as provided on product labeling. The stability studies you conducted as per protocol STB-22-0029 and STB-22-0030 titled "Stability Study Protocol for Regener-Eyes Ophthalmic Solution, (b) (4) mL Professional Strength" failed to meet defined objectives for example:

STB-22-0029 - (b) (4) Accelerated Studies at (b) (4)

AMENDMENT 1

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

a) Failed container closure integrity test (CCIT) at (b) (4) accelerated stability)
b) Failed CCIT at (b) (4) accelerated stability)
c) CCIT was discontinued and not tested from (b) (4) through (b) (4) accelerated stability)

STB-22-0030 - (b) (4) Temperature Studies at (b) (4)

a) 7.7 pH value (range (b) (4) at (b) (4) RT stability)
b) Failed CCIT at (b) (4) RT stability)
c) CCIT was discontinued and not tested for (b) (4) RT stability)

OBSERVATION 4

Container closure systems do not provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.

Specifically, you manufacture the products Regener-Eyes PRO and Regener-Eyes LITE ophthalmic eye drops (3ml). The final product container (eye dropper) utilized to hold these products was observed as not being for single use nor does it have a backflow prevention design to prevent microbial contamination of the product after being opened.

OBSERVATION 5

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

AMENDMENT 1

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

a) Your environmental monitoring program currently utilizes (b) (4) an active air monitor, surface sampling, and personnel monitoring within all (b) (4) of your biological safety cabinets (BSCs) you identify as ISO-5 to monitor environmental conditions within the critical area used to manufacture and fill both Regener-Eyes PRO and Regener-Eyes LITE ophthalmic eye drops (3ml). When asked during the inspection on 06/22/2023, your Vice President of Manufacturing stated that there have not been environmental excursions within your BSCs during manufacturing, but it was observed within your monitoring records that you currently have not established microbial action limits for your BSCs in order to identify and investigate any environmental excursions. Both Regener-Eyes PRO and Regener-Eyes LITE are purported to be sterile.

b) You do not conduct growth promotion testing to verify that the (b) (4) media utilized for environmental monitoring within your BSCs and cleanroom can support growth of microorganisms.

c) You have not defined environmental action limits and alert levels for non-viable, active air, surface sampling, and personnel monitoring within procedure R-MICRO-11 (ver. 1 - 12/29/2022) titled "Environmental Monitoring Program."

OBSERVATION 6

Samples taken to determine conformance to appropriate written specifications for the acceptance of each lot within each shipment of drug product containers are not representative.

Specifically, your firm conducts a (b) (4) sampling approach to visually inspect (b) (4) bottles of Regener-Eyes PRO and Regener-Eyes LITE ophthalmic solution regardless of lot size. For example, for

AMENDMENT 1

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Travis S Bradley, Investigator Samantha J Pinizzotto, Investigator Ivan E Reyes, Investigator	X Travis S Bradley Investigator Signed By: Travis S. Bradley -S Date Signed: 06-30-2023 10:29:06	6/30/2023

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

Regener-Eyes PRO lot 031423A, lot size (b) (4) units, your (b) (4) sampling plan calls for visually inspecting only (b) (4) units total without rationale. Additionally, your firm's visual inspection instructions and procedures found that visually inspecting the container for particulates was not referenced.

OBSERVATION 7

Buildings used in the manufacture, processing, packing, or holding of a drug product do not have the suitable to facilitate cleaning, maintenance, and proper operations.

Specifically, on 06/20/2023, while observing the (b) (4) cleanrooms (b) (4) you identify as ISO-7 used for manufacturing Regener-Eyes PRO and Regener-Eyes LITE ophthalmic eye drops it was observed that:

- The walls and ceiling within cleanroom (b) (4) was observed to not be of suitable construction containing uneven surfaces, false doors (no longer operational with uneven frames), and protruding light fixtures.

- Cleanroom (b) (4) does not contain adequate low wall exhaust vents to support unidirectional airflow and flush dirty air out of the cleanroom you identify as ISO-7 and minimize turbulence. It was observed that on the lower wall adjacent to the BSC utilized for manufacturing product, five slats were cut into the side of the cleanroom wall to mimic a low wall exhaust. These slats were observed to directly open into the unclassified area outside of the cleanroom.

OBSERVATION 8

AMENDMENT 1

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

Written procedures are not established for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

Specifically, your method for cleaning and sanitizing contact surfaces within your (b) (4) BSCs you identify as ISO-5 and supporting cleanrooms (b) (4) you identify as ISO-7 utilized to manufacture both Regener-Eyes PRO and Regener-Eyes LITE ophthalmic solution eye drops (3ml) has not been adequately validated. No validation study has been conducted to substantiate that your cleaning agents can effectively clean and sanitize contact surfaces within the BSC and supporting cleanrooms. Additionally, the EM media utilized to support your current cleaning validation (Document: CV-01) was not tested for growth promotion nor were positive controls used to demonstrate that the media you use can support the growth of microorganisms.

OBSERVATION 9

You did not retain reserve samples for drug products for one year after the expiration dates of the drug products.

Specifically, it was observed that retain samples pertaining to your Regener-Eyes PRO and Regener Eyes LITE amniotic fluid ophthalmic eye drops which you reported to FDA were discontinued in June 2021 were not retained.

OBSERVATION 10

Specific identification tests are not conducted on components that have been accepted based on the supplier's report of analysis.

AMENDMENT 1

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Travis S Bradley, Investigator Samantha J Pinizzotto, Investigator Ivan E Reyes, Investigator X Travis S Bradley Investigator Signed By: Travis S. Bradley -S Date Signed: 06-30-2023 10:29:06	6/30/2023

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

Specifically, your firm does not conduct an identity test when receiving lots of sterile (b) (4) sodium chloride used to formulate the (b) (4) component used in the production of Regener-Eyes PRO and Regener-Eyes LITE ophthalmic solution eye drops (3ml). On 06/20/2023, your Senior VP of Quality stated that your firm does not conduct identity tests for sterile (b) (4) sodium chloride used to manufacture your (b) (4) solution contained in both products.

OBSERVATION 11

The responsibilities and procedures applicable to the quality control unit are not fully followed.

Specifically, the following critical deficiencies were observed regarding your quality unit (this list is not all-inclusive):

a) During review of your initial media fill studies conducted to validate your aseptic manufacturing process for both Regener-Eyes PRO and Regener-Eyes LITE ophthalmic solution eye drops (3ml) conducted (b) (4) it was observed that (b) (4) of the (b) (4) media fill runs failed due to contamination being identified within filled containers. Both failures were not investigated to determine the cause of the contamination or whether there was a potential impact of final product lots manufactured prior to the study. Additionally, you did not attempt to identify the species of the microorganism after receiving the testing results from your contracted sterility testing laboratory.

b) You currently have not established environmental monitoring action levels for viable passive air sampling, active air sampling, surface sampling, and personnel monitoring within the (b) (4) BSCs you identify as ISO-5 utilized for manufacturing Regener-Eyes PRO and Regener-Eyes LITE ophthalmic solution eye drops (3ml).

AMENDMENT 1

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Travis S Bradley, Investigator Samantha J Pinizzotto, Investigator Ivan E Reyes, Investigator X Travis S Bradley Investigator Signed By: Travis S. Bradley -S Date Signed: 06-30-2023 10:29:06	6/30/2023

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

c) Since commencing manufacturing operations for Regener-Eyes PRO and Regener-Eyes LITE ophthalmic solution eye drops (3ml), it was observed that a combined (b) (4) lots of both products were identified with pH levels greater than your defined pH range of (b) (4) equating to 27% of all lots manufactured. All (b) (4) batches were observed to have not been investigated.

d) Your analytical laboratory procedure LAB-028 titled "Analytical Laboratory Investigation Report" allows retesting for Regener-Eyes PRO and Regener-Eyes LITE out of specification (OOS) results without a root cause.

e) You failed to maintain records for the Regener-Eyes PRO and Regener-Eyes LITE ophthalmic solution eye drops, you manufactured containing amniotic fluid prior to June 2021 (two-year shelf life for both products). Records identifying complaints, manufacturing procedures, receiving records, and inventory logs were requested but these records cannot be located as per your Senior Director of Quality and Chief Strategist.

OBSERVATION 12

Equipment and utensils are not maintained at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically, review of the qualification records for the BSCs (b) (4) claimed to be ISO-5 and cleanrooms (b) (4) claimed to be ISO-7 used to manufacture Regener-Eyes PRO and Regener-Eyes LITE, did not include dynamic qualifications of (b) (4) the BSCs and supporting cleanrooms. Your Senior VP of Quality stated that the qualification of your cleanrooms was conducted at static conditions and was not challenged under fully operational conditions. Additionally, it was observed that you currently only conduct (b) (4) HEPA filter integrity tests pertaining to the HEPA filters utilized within your cleanrooms.

AMENDMENT 1

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Travis S Bradley, Investigator Samantha J Pinizzotto, Investigator Ivan E Reyes, Investigator	X Travis S Bradley Investigator Signed By: Travis S. Bradley -S Date Signed: 06-30-2023 10:29:06	6/30/2023

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

OBSERVATION 13

Laboratory records are deficient in that they do not include a complete record of all data obtained during testing.

Specifically, your firm conducts (b) (4) or (b) (4) on your High-Performance Liquid Chromatography (HPLC) glycerin samples for Regener-Eyes PRO and Regener-Eyes LITE ophthalmic eye drops (3ml) prior to analytical release testing within the HPLC. On 06/26/2023, it was observed that the firm's chemist conducts (b) (4) prior to running the official samples. These (b) (4) are not outlined within your procedures ATM-002 (ver. 2 - 12/07/2022) titled "Glycerin Analysis by HPLC in Regener-Eyes PRO and LITE" and observed to not be part of the official testing records reviewed and approved by your quality unit. Per your Senior VP of Quality, these (b) (4) have been conducted for every lot tested of Regener-Eyes PRO (b) (4) lots) and Regener-Eyes LITE ((b) (4) lots) since commencing analytical testing operations on 08/22/2022.

OBSERVATION 14

All records of production associated with a batch of drug product were not maintained at least one (1) year after the expiration date.

Specifically, during the inspection on 06/22/2023, in response to a request for records pertaining to Regener-Eyes PRO and Regener-Eyes LITE products derived from amniotic fluid (discontinued in ~06/2021 as per your Chief Strategist), your Chief Strategist stated that she could not locate any records such as complaint records, distribution records, receiving records, storage records, and manufacturing records. She further stated that she could not remember where the records went or if they were destroyed or not. Regener-Eyes PRO and Regener-Eyes LITE manufactured with amniotic fluid components was labeled with a two-year shelf life as per your Chief Strategist.

OBSERVATION 15

Batch production and control records do not include the specific identification of each batch of component used for each batch of drug product produced.

AMENDMENT 1

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Travis S Bradley, Investigator Samantha J Pinizzotto, Investigator Ivan E Reyes, Investigator	X Travis S Bradley Investigator Signed By: Travis S. Bradley -S Date Signed: 06-30-2023 10:29:06	6/30/2023

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768 orabioinspectionalcorrespondence@fda.hhs.gov	6/20/2023-6/30/2023* FEI NUMBER 3011320041

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Dr. Carl R. Harrell, Medical Director	
FIRM NAME Regenerative Processing Plant, LLC	STREET ADDRESS 34176 Us Highway 19 N
CITY, STATE, ZIP CODE, COUNTRY Palm Harbor, FL 34684-2144	TYPE ESTABLISHMENT INSPECTED Drug Manufacturer

Specifically, during the inspection on 06/20/2023, your owner and Medical Director stated that the (b) (4) manufactured as an (b) (4) for both Regener-Eyes PRO and Regener-Eyes LITE ophthalmic eye drops (3ml) contains only sterile (b) (4) sodium chloride. However, completed batch records for Regener-Eyes PRO and Regener-Eyes LITE do not identify that sterile (b) (4) sodium chloride is used as a component within the manufacture of your Regener-Eyes PRO and Regener-Eyes LITE products.

***DATES OF INSPECTION**

6/20/2023(Tue), 6/21/2023(Wed), 6/22/2023(Thu), 6/23/2023(Fri), 6/26/2023(Mon), 6/28/2023(Wed), 6/30/2023(Fri)

X Samantha J Pinizzotto
Investigator
Signed By: Samantha J. Pinizzotto -S
Date Signed: 06-30-2023 10:29:47

AMENDMENT 1

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Travis S Bradley, Investigator Samantha J Pinizzotto, Investigator Ivan E Reyes, Investigator	X Travis S Bradley Investigator Signed By Travis S. Bradley -S Date Signed 06-30-2023 10 29 06	6/30/2023

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."