the dry eye foundation

26273 Twelve Trees Lane NW | Poulsbo Washington 98370 | 1-800-484-0244 | info@dryeyefoundation.org

OPEN LETTER TO THE FOOD AND DRUG ADMINISTRATION

Manipulation of the FDA Non-Prescription Drug Database for Marketing Purposes

Dear FDA Center for Drug Evaluation and Research, Office of Compliance:

Re: Regenerative Processing Plant, Regener-Eyes LLC, Regener-Eyes Pro, Regener-Eyes Lite

The Dry Eye Foundation is a 501(c)(3) nonprofit organization serving the ocular surface disease and ocular surface pain patient communities. Our activities include public education about eye drop safety. (1) (2)

We are writing to urge you, as a matter of public safety, to review and remove two biologic drugs from the Food and Drug Administration's public over-the-counter drug listing database. We have communicated with the FDA regarding this matter in the past (3).

Regener-Eyes products are unapproved biologic drugs

On April 6, 2022, FDA's Center for Biologics Evaluation and Research (Jurisdiction Office) shared with us their position that Regener-Eyes eye drops *are regulated by FDA* and that amniotic fluid products *require premarket approval in order to be marketed for any medical application*. (4)

On October 5, 2023, CBER sent an Untitled Letter to Regener-Eyes LLC stating, among other things: "Your product is not the subject of an approved biologics license application (BLA), nor is there an IND in effect for your product." (5)

On April 10, 2023, CBER issued a Public Safety Notification on Amniotic Fluid Eye Drops with specific reference to Regener-Eyes LLC. (6) This notification stated, among other things:

> *"...manufacturers are marketing and distributing amniotic fluid eyedrops to treat, mitigate, or cure diseases or conditions such as dry eye disease without the required premarket review and approval, raising potential significant safety concerns."*

Regener-Eyes products are listed as OTC drugs on DailyMed

OTC drug entries for Regener-Eyes Lite and Regener-Eyes Pro eye drops have been active on DailyMed since 2021. (Attachment A)

Each Regener-Eyes OTC drug listing displays an inactive ingredient with no UNII (Attachment B) i.e. ingredient not found in the FDA's ingredient database. In the first version of each listing, the ingredient with no UNII is "d-MAPPS™", identifiable as a biologic substance (amniotic fluid). (7) In the second and third iterations of the listing, introduced in 8/2022 and 1/2023 respectively, the ingredient with no UNII is "Tonicity Solution", an unknown substance which the company describes as proprietary. (Attachment C)

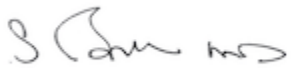
Regener-Eyes cites OTC listings as evidence of FDA regulatory compliance

In order to substantiate the safety and efficacy of its products, Regener-Eyes has long represented to the public and to physicians that its products are OTC drugs that comply with all FDA regulatory laws. (Attachment D)

In a recent marketing email (Attachment E), Regener-Eyes claims that their products were recently "reviewed and granted an OTC Drug Monograph Final status from the FDA with an indication To Relieve Dryness of the Eye", and the email contains a hyperlink (8) to the National Drug Code Directory as evidence. *Regener-Eyes describes this imputed FDA action as a "huge milestone".*

As a matter of public safety, we urge you to immediately remove Regener-Eyes' drug listings.

Sincerely,



Sandra Brown, MD
Medical Advisor

Rebeca Petris
Executive Director

Recipients

Center for Drug Evaluation and Research

Office of Compliance

Jill Furman, J.D. - Director
Mike Levy, J.D. - Deputy Director

Office of Unapproved Drugs & Labeling Compliance

Carolyn E. Becker, J.D. - Director
Tina Smith, M.S. - Acting Director, Deputy Director

Office of Nonprescription Drugs, Division of Nonprescription Drugs II

Karen Murry, M.D. - Director (acting)
Karen Hicks, M.D. - Deputy Director

Copy to

Center for Biologics Evaluation and Research

Office of Compliance and Biologics Quality

Melissa Mendoza, J.D. - Director

Notes

(1) Eyedropsafety.org
(2) Biologiceyedrops.org
(3) Email communication from RP to CBERProductJurisdiction.fda.hhs.gov on 4/14/2022; telephone and email communications from SMB 2Q/3Q 2022; email communication from RP to CDEROUDLCPMTRACK@cder.fda.gov on 10/24/22 with receipt acknowledged on 10/7/22
(4) Email communication received by RP from CBERProductJurisdiction.fda.hhs.gov on 4/6/2022
(5) Untitled Letter, 10/5/2022
(6) Public Safety Notification on Amniotic Fluid Eyedrops 4/10/2023
(7) C. R. Harrell, 2019. Therapeutic Potential of Amniotic Fluid Derived Mesenchymal Stem Cells Based on their Differentiation Capacity and Immunomodulatory Properties Current Stem Cell Research & Therapy
(8) https://www.accessdata.fda.gov/scripts/cder/ndc/index.cfm

Attachment A - FDA OTC Listing History

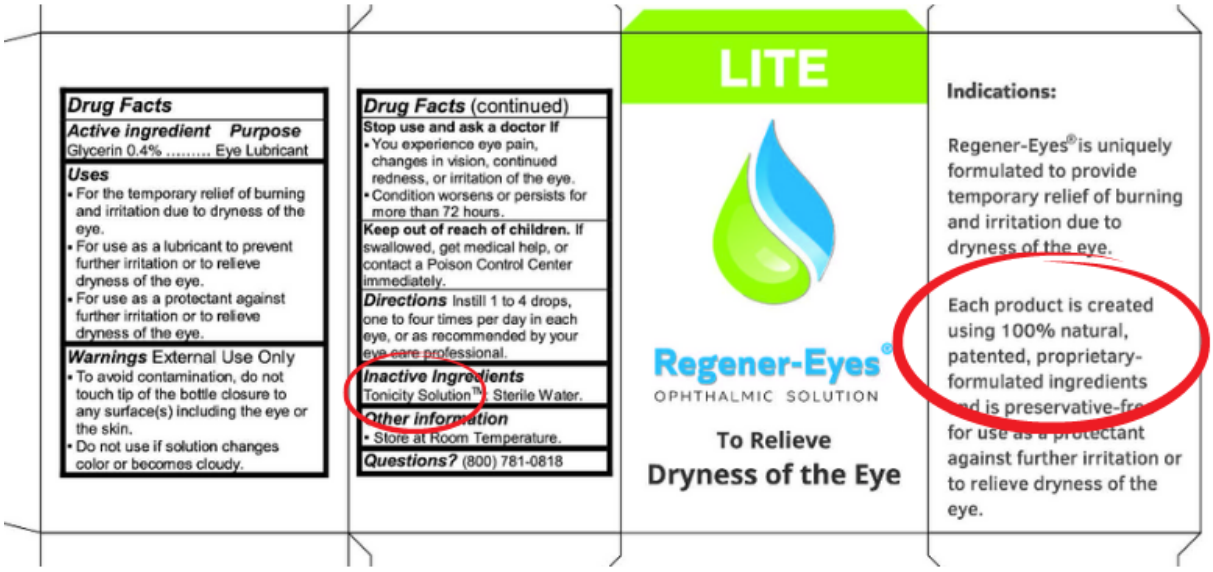
REGENEREYES	**Lite**	**Pro**
Archived Version 1	82305-002	82305-001
Revised	11/2021	10/2021
Marketing start	3/31/22	3/31/22
Marketing end	-	-
Archived Version 2	82305-002	82305-001
Revised	9/2022	9/2022
Marketing start	4/29/21	3/31/22
Marketing end	4/29/21	4/29/22
REGENER-EYES	**Lite**	**Pro**
Archived Version 1	82305-006	
Revised	8/2022	
Marketing start	8/24/22	
Marketing end	-	
Archived Version 2, Version 3	82305-004	
Revised	8/20/22	
Marketing start	8/24/22	
Marketing end	-	
Archived Version 4	82305-006	82305-003
Revised	12/2022	12/2022
Marketing start	8/24/22	8/24/22
Marketing end		
Active version (as of 5/10/23)	82305-006-01	82305-003-01
Revised	1/2023	1/2023
Marketing start	8/24/22	8/24/22
Marketing end	-	-

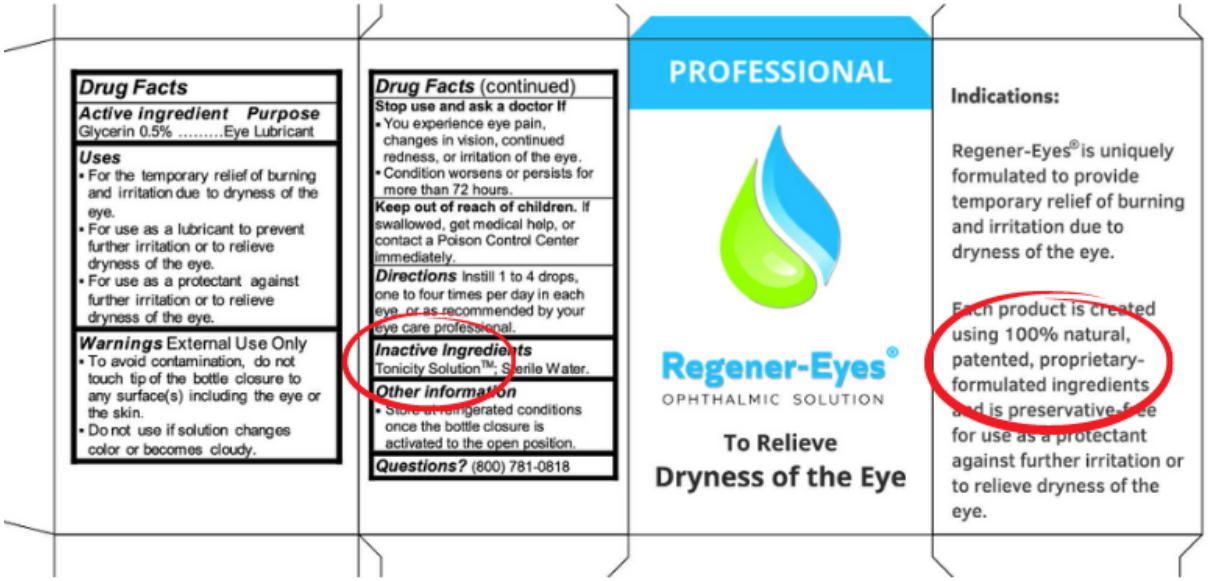
Attachment B - Ingredients without UNIIs

Regenereyes Lite (Archived) 82305-002 d-MAPPS ™ and 0.9% Sodium Chloride USP. eye care professional. **Inactive Ingredients** d-MAPPS™ and 0.9% Sodium Chloride USP. **Other information**	Regenereyes Pro (Archived) 82305-001 **Inactive Ingredients** d-MAPPS ™ and 0.9% Sodium Chloride USP. by your eye care professional. **Inactive Ingredients** d-MAPPS™ and 0.9% Sodium Chloride USP. **Other information**
Regener-Eyes Lite (Archived) 82305-006 ***Inactive ingredients*** Tonicity Solution ™; Sterile Water. eye care professional. **Inactive Ingredients** Tonicity Solution™; Sterile Water. **Other information**	Regener-Eyes Pro (Archived) 82305-003 ***Inactive Ingredients*** Tonicity Solution ™; Sterile Water. eye care professional. **Inactive Ingredients** Tonicity Solution™; Sterile Water. **Other information**
Regener-Eyes Lite (Active) 82305-006-01 INACTIVE INGREDIENTS Sterile Water, Tonicity Solution Sodium Chloride. eye care professional. **Inactive Ingredients** Tonicity Solution™; Sterile Water. **Other information**	Regener-Eyes Pro (Active) 82305-003-01 INACTIVE INGREDIENTS Sterile Water, Tonicity Solution Sodium Chloride eye care professional. **Inactive Ingredients** Tonicity Solution™; Sterile Water. **Other information**

Attachment C: Proprietary ingredient in current listings

Current DailyMed listings (as of 5/12/23)





Attachment D: Regener-Eyes LLC's public claims about its FDA regulatory status

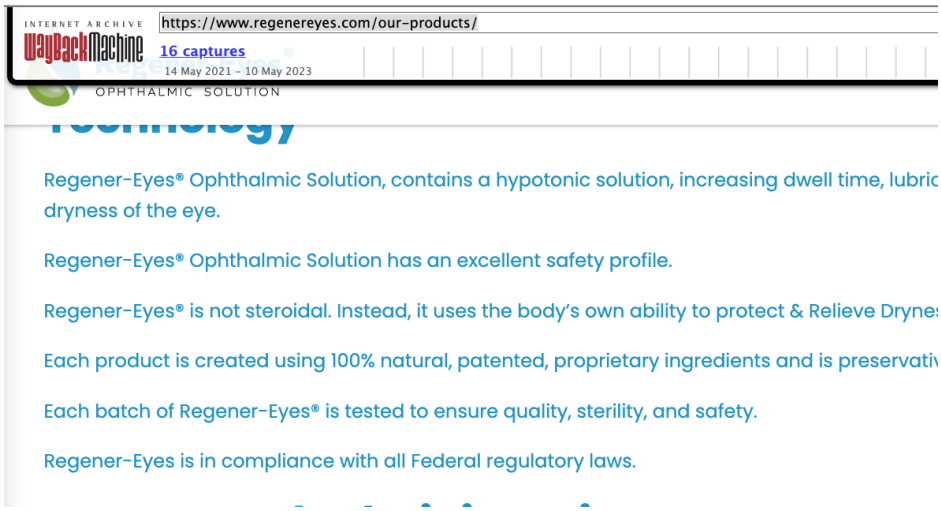
July 2021: Eyeworld White Paper

Marguerite McDonald MD and Carl Randall Harrell [CMH is Chairman and CEO of Regener-Eyes LLC), 7/2021, Therapeutic potential of Regener-Eyes Ophthalmic Solution in the treatment of dry eye disease, Eyeworld

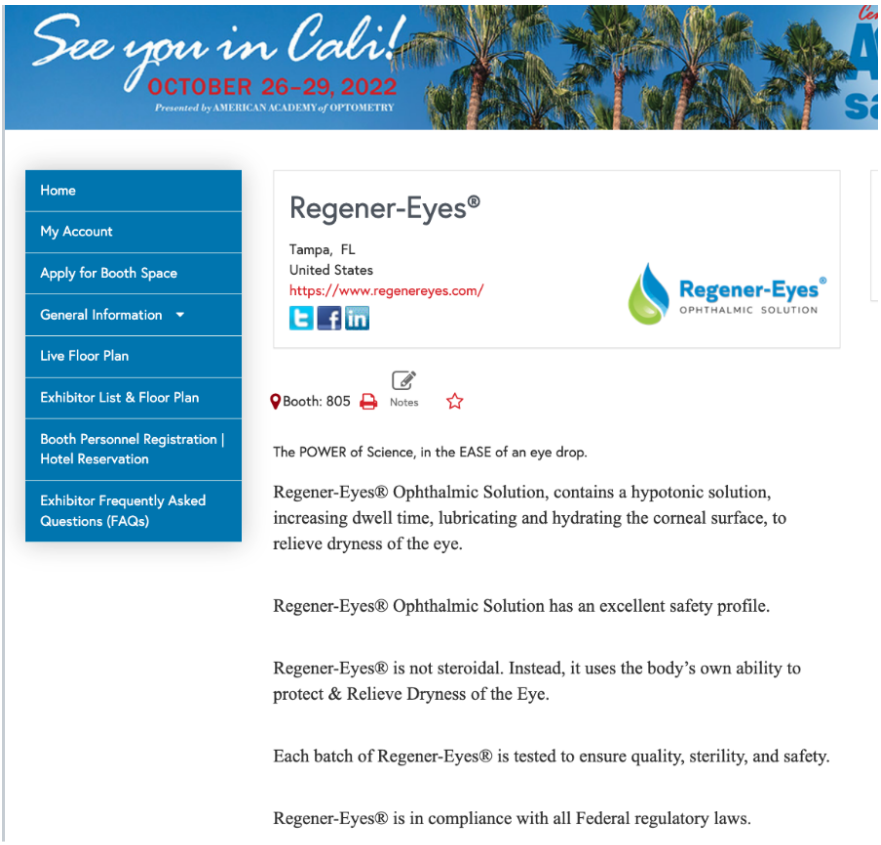
Excerpt:

Regener-Eyes® is an engineered biological product derived from human placental-based biomaterials, manufactured under current Good Manufacturing Practices (cGMP), regulated and reviewed by the Food and Drug Administration (FDA).[9] Regener-Eyes® incorporates Regenerative Processing Plant's (RPP) proprietary patented sterilization process to provide for a safe, sterile product for clinical use.[9] Regener-Eyes® is enriched with AF-MSC-Exos containing AF-MSC-derived immunoregulatory, angio-modulatory and

September 30, 2022: regenereyes.com/our-products (archived version)



October 2022: American Academy of Optometry Exhibitor Profile



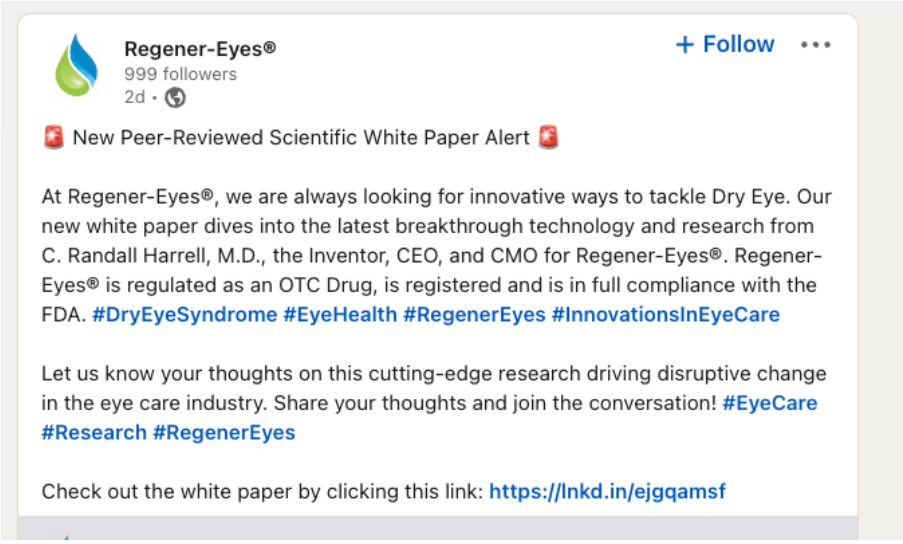
May 1, 2023: Press release

NEWS PROVIDED BY
Regener-Eyes
May 01, 2023, 08:00 ET

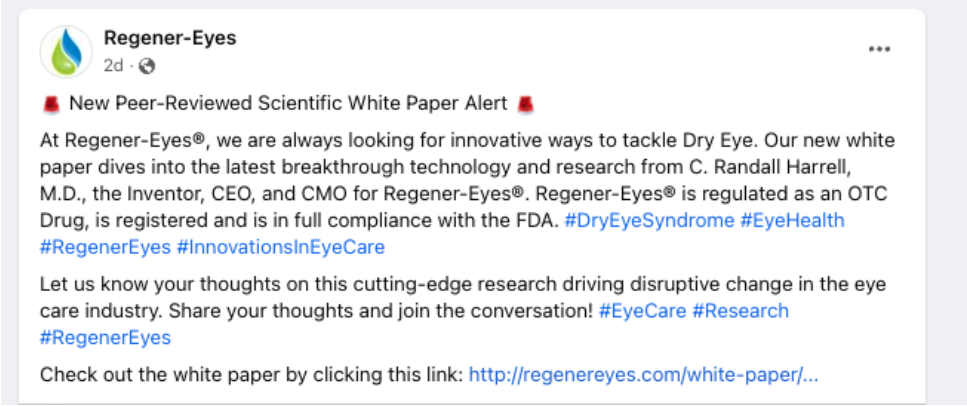
SHARE THIS ARTICLE

TAMPA, Fla., May 1, 2023 /PRNewswire/ -- Regener-Eyes® is regulated as an OTC drug product that is registered and in full compliance with all FDA regulations. The Regener-Eyes® family is excited to announce that our Founder, CEO, and Chief Medical Officer, C. Randall Harrell, M.D., has just published a peer-reviewed scientific white paper on Regener-Eyes®, an ophthalmic solution To Relieve Dryness of the Eye.

May 8, 2023: LinkedIn post



May 8, 2023: Facebook post



May 12, 2023: regenereyes.com/our-products

Attachment E: Regener-Eyes 5/5/22 email

5/5/2022 email, containing hyperlink to the National Drug Code Directory
https://www.accessdata.fda.gov/scripts/cder/ndc/index.cfm

SETTING THE RECORD STRAIGHT

We are excited to share some great news that Regener-Eyes® was recently reviewed and granted an OTC Drug Monograph Final status from the FDA with an indication To Relieve Dryness of the Eye. Regener-Eyes® is regulated as an OTC Drug that is registered and in full compliance with all FDA regulations.

Recently, one of the publications, Glance by Eyes On Eyecare (see below), updated information to now show our OTC Drug Monograph Final status update.

Regener-Eyes Ophthalmic Solution was awarded an over-the-counter (OTC) drug indication to relieve dryness of the eye in August 2022.

The OTC Monograph was the subject of a final administrative order by the FDA, meaning that the non-prescription drug is "generally recognized as safe and effective (GRASE) for its intended use."

UPDATE 5/1/23: This section has been updated to reflect the status of these drops and the companies' responses.

This is a **HUGE MILESTONE** for us at Regener-Eyes®, we are grateful for the physician partnerships and all of the wonderful patients that we have been able to help with our first in class products.

Regener-Eyes® is regulated as an OTC drug that is registered and in full compliance with all FDA regulations.

The POWER of Science, in the EASE of an Eye Drop™

For more Information or
to speak with a Product Specialist CALL 877-206-0706