



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)

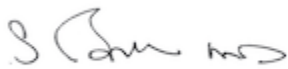
Regener-Eyes cites OTC listings as evidence of FDA regulatory compliance

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

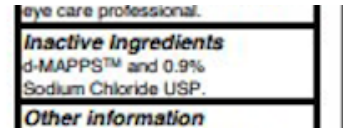
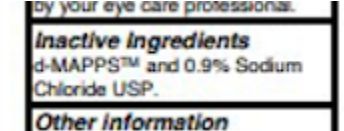





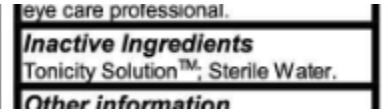
Notes

- (1) Eyedropsafety.org
- (2) Biologicseyedrops.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@cdcr.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 UNIs

<p>RegenerEyes Lite (Archived) 82305-002</p> <p>d-MAPPS™ and 0.9% Sodium Chloride USP.</p> 	<p>RegenerEyes Pro (Archived) 82305-001</p> <p>Inactive Ingredients d-MAPPS™ and 0.9% Sodium Chloride USP.</p> 
<p>Regener-Eyes Lite (Archived) 82305-006</p> <p>Inactive ingredients Tonicity Solution™; Sterile Water.</p> 	<p>Regener-Eyes Pro (Archived) 82305-003</p> <p>Inactive Ingredients Tonicity Solution™; Sterile Water.</p> 
<p>Regener-Eyes Lite (Active) 82305-006-01</p> <p> INACTIVE INGREDIENTS</p> <p>Sterile Water, Tonicity Solution Sodium Chloride.</p> 	<p>Regener-Eyes Pro (Active) 82305-003-01</p> <p> INACTIVE INGREDIENTS</p> <p>Sterile Water, Tonicity Solution Sodium Chloride</p> 

Attachment C: Proprietary ingredient in current listings

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

<p>Drug Facts</p> <p>Active ingredient Purpose Glycerin 0.4% Eye Lubricant</p> <p>Uses</p> <ul style="list-style-type: none"> For the temporary relief of burning and irritation due to dryness of the eye. For use as a lubricant to prevent further irritation or to relieve dryness of the eye. For use as a protectant against further irritation or to relieve dryness of the eye. <p>Warnings External Use Only</p> <ul style="list-style-type: none"> To avoid contamination, do not touch tip of the bottle closure to any surface(s) including the eye or the skin. Do not use if solution changes color or becomes cloudy. 	<p>Drug Facts (continued)</p> <p>Stop use and ask a doctor if</p> <ul style="list-style-type: none"> You experience eye pain, changes in vision, continued redness, or irritation of the eye. Condition worsens or persists for more than 72 hours. <p>Keep out of reach of children. If swallowed, get medical help, or contact a Poison Control Center immediately.</p> <p>Directions Instill 1 to 4 drops, one to four times per day in each eye, or as recommended by your eye care professional.</p> <p>Inactive Ingredients Tonicity Solution™, Sterile Water.</p> <p>Other information</p> <ul style="list-style-type: none"> Store at Room Temperature. <p>Questions? (800) 781-0818</p>	<p style="text-align: center;">LITE</p>  <p style="text-align: center;">Regener-Eyes® OPHTHALMIC SOLUTION</p> <p style="text-align: center;">To Relieve Dryness of the Eye</p>	<p>Indications:</p> <p>Regener-Eyes® is uniquely formulated to provide temporary relief of burning and irritation due to dryness of the eye.</p> <p>Each product is created using 100% natural, patented, proprietary-formulated ingredients and is preservative-free for use as a protectant against further irritation or to relieve dryness of the eye.</p>
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<p>Drug Facts</p> <p>Active ingredient Purpose Glycerin 0.5% Eye Lubricant</p> <p>Uses</p> <ul style="list-style-type: none"> For the temporary relief of burning and irritation due to dryness of the eye. For use as a lubricant to prevent further irritation or to relieve dryness of the eye. For use as a protectant against further irritation or to relieve dryness of the eye. <p>Warnings External Use Only</p> <ul style="list-style-type: none"> To avoid contamination, do not touch tip of the bottle closure to any surface(s) including the eye or the skin. Do not use if solution changes color or becomes cloudy. 	<p>Drug Facts (continued)</p> <p>Stop use and ask a doctor if</p> <ul style="list-style-type: none"> You experience eye pain, changes in vision, continued redness, or irritation of the eye. Condition worsens or persists for more than 72 hours. <p>Keep out of reach of children. If swallowed, get medical help, or contact a Poison Control Center immediately.</p> <p>Directions Instill 1 to 4 drops, one to four times per day in each eye, or as recommended by your eye care professional.</p> <p>Inactive Ingredients Tonicity Solution™, Sterile Water.</p> <p>Other information</p> <ul style="list-style-type: none"> Store at refrigerated conditions once the bottle closure is activated to the open position. <p>Questions? (800) 781-0818</p>	<p style="text-align: center;">PROFESSIONAL</p>  <p style="text-align: center;">Regener-Eyes® OPHTHALMIC SOLUTION</p> <p style="text-align: center;">To Relieve Dryness of the Eye</p>	<p>Indications:</p> <p>Regener-Eyes® is uniquely formulated to provide temporary relief of burning and irritation due to dryness of the eye.</p> <p>Each product is created using 100% natural, patented, proprietary-formulated ingredients and is preservative-free for use as a protectant against further irritation or to relieve dryness of the eye.</p>
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Attachment D: Regener-Eyes LLC's public claims about its FDA regulatory status

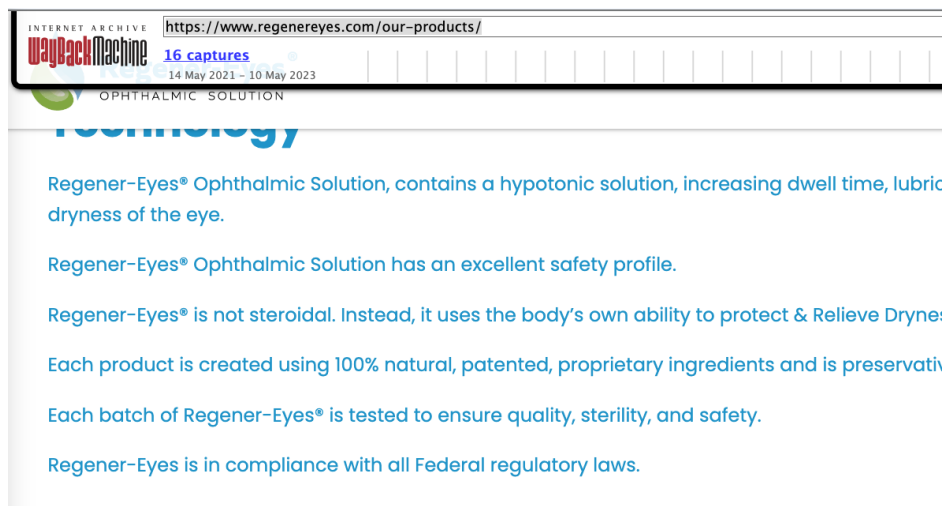
July 2021: Eyeworld White Paper

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](https://www.regenereyes.com/our-products) (archived version)



The screenshot shows the top portion of a website page. At the top, there is a navigation bar with the text "INTERNET ARCHIVE" and a URL "https://www.regenereyes.com/our-products/". Below this is a "Wayback Machine" logo and the text "16 captures" and "14 May 2021 - 10 May 2023". The main content area features the word "technology" in a large, stylized font. Below this, there are several lines of text describing the product: "Regener-Eyes® Ophthalmic Solution, contains a hypotonic solution, increasing dwell time, lubric dryness of the eye.", "Regener-Eyes® Ophthalmic Solution has an excellent safety profile.", "Regener-Eyes® is not steroidal. Instead, it uses the body's own ability to protect & Relieve Dryne:", "Each product is created using 100% natural, patented, proprietary ingredients and is preservati", "Each batch of Regener-Eyes® is tested to ensure quality, sterility, and safety.", and "Regener-Eyes is in compliance with all Federal regulatory laws."




October 2022: American Academy of Optometry Exhibitor Profile


See you in Cali!
OCTOBER 26-29, 2022
Presented by AMERICAN ACADEMY OF OPTOMETRY



- Home
- My Account
- Apply for Booth Space
- General Information ▾
- Live Floor Plan
- Exhibitor List & Floor Plan
- Booth Personnel Registration | Hotel Reservation
- Exhibitor Frequently Asked Questions (FAQs)

Regener-Eyes®

Tampa, FL
United States
<https://www.regenereyes.com/>



Booth: 805  

The POWER of Science, in the EASE of an eye drop.

Regener-Eyes® Ophthalmic Solution, contains a hypotonic solution, increasing dwell time, lubricating and hydrating the corneal surface, to relieve dryness of the eye.

Regener-Eyes® Ophthalmic Solution has an excellent safety profile.

Regener-Eyes® is not steroidal. Instead, it uses the body's own ability to protect & Relieve Dryness of the Eye.

Each batch of Regener-Eyes® is tested to ensure quality, sterility, and safety.

Regener-Eyes® is in compliance with all Federal regulatory laws.

May 1, 2023: [Press release](#)

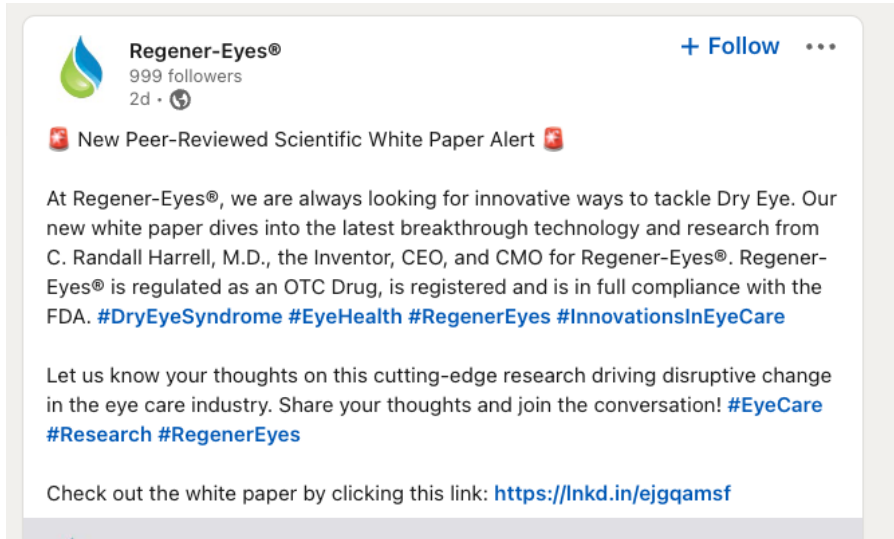
NEWS PROVIDED BY
Regener-Eyes →
May 01, 2023, 08:00 ET

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



Regener-Eyes® 999 followers
2d · 🌐

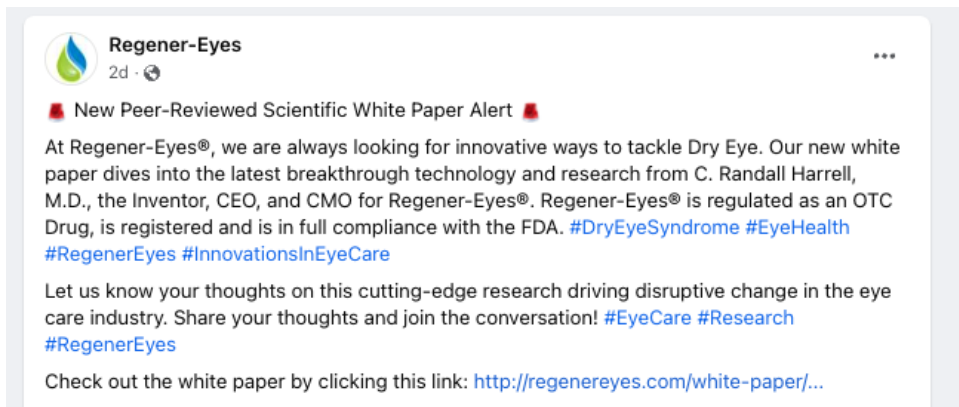
New Peer-Reviewed Scientific White Paper Alert

At Regener-Eyes®, we are always looking for innovative ways to tackle Dry Eye. Our new white paper dives into the latest breakthrough technology and research from C. Randall Harrell, M.D., the Inventor, CEO, and CMO for Regener-Eyes®. Regener-Eyes® is regulated as an OTC Drug, is registered and is in full compliance with the FDA. [#DryEyeSyndrome](#) [#EyeHealth](#) [#RegenerEyes](#) [#InnovationsInEyeCare](#)

Let us know your thoughts on this cutting-edge research driving disruptive change in the eye care industry. Share your thoughts and join the conversation! [#EyeCare](#) [#Research](#) [#RegenerEyes](#)

Check out the white paper by clicking this link: <https://lnkd.in/ejqgamsf>

May 8, 2023: Facebook post



Regener-Eyes
2d · 🌐

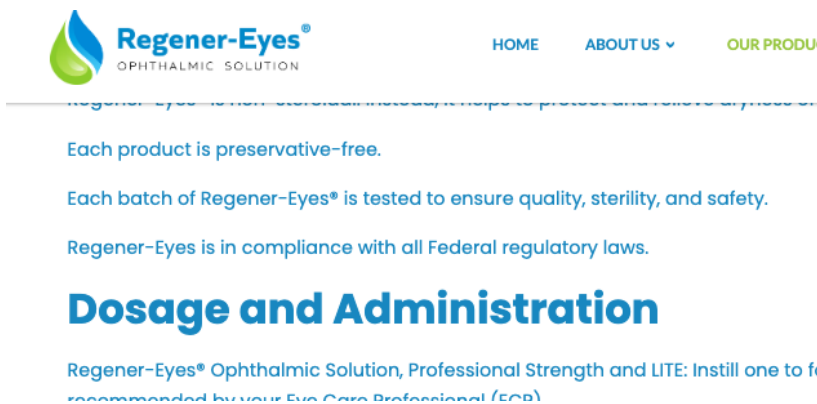
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At Regener-Eyes®, we are always looking for innovative ways to tackle Dry Eye. Our new white paper dives into the latest breakthrough technology and research from C. Randall Harrell, M.D., the Inventor, CEO, and CMO for Regener-Eyes®. Regener-Eyes® is regulated as an OTC Drug, is registered and is in full compliance with the FDA. [#DryEyeSyndrome](#) [#EyeHealth](#) [#RegenerEyes](#) [#InnovationsInEyeCare](#)

Let us know your thoughts on this cutting-edge research driving disruptive change in the eye care industry. Share your thoughts and join the conversation! [#EyeCare](#) [#Research](#) [#RegenerEyes](#)

Check out the white paper by clicking this link: <http://regenereyes.com/white-paper/...>

May 12, 2023: [regenereyes.com/our-products](https://www.regenereyes.com/our-products)



Regener-Eyes®
OPHTHALMIC SOLUTION

HOME ABOUT US ▾ OUR PRODUCTS

Each product is preservative-free.

Each batch of Regener-Eyes® is tested to ensure quality, sterility, and safety.

Regener-Eyes is in compliance with all Federal regulatory laws.

Dosage and Administration

Regener-Eyes® Ophthalmic Solution, Professional Strength and LITE: Instill one to five drops (as recommended by your Eye Care Professional (ECP))

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

