New Studies Support Safety of Isopropyl Cloprostenate in Cosmetics

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CIR Expert Panel Meeting
December 4, 2023

New Safety Studies

- 8-Month /120 Subject Clinical Study run on a lash serum containing 0.0044% IC (the "Clinical Study").
  - **General safety:** Safe for use by both contact and non-contact lens wearers.
  - **Ocular irritation:** Slight potential for transient ophthalmological irritation.
  - **Ocular pigmentation:** No statistically significant difference in visible color of iris on RGB scale after 8 months.
  - **Periorbital Volume:** No change in periorbital volume after 8 months.

- Intraocular Pressure Assay run on a lash serum containing 0.005% IC (the "IOP Assay").
  - **Intraocular pressure:** No statistically significant difference in intraocular pressure after 28 days.

- Toxicological Safety Assessment evaluating safety of lash serums containing up to 0.005% IC (the "Tox Report").
  - **Systemic toxicity:** low risk of potential systemic toxicity due to *de minimis* exposure.

New Safety Studies Substantiate Safety

- We believe new safety studies **meet MoCRA standards** and **support the safe use** of IC in cosmetic lash serums containing up to **0.005%** IC.

- Results consistent with ***de minimus* exposure** to IC.
  - **Amount of IC per application**: 0.0000084 mg.
  - **Site of application**: upper lash line only.
  - **Method of application:** fine brush applicator optimizes precise application of small amount of serum.
  - **Formulation, packaging and directions for use**: designed to prevent ocular exposure.
    - If serum does get in eye, consumers instructed to immediately rinse with cool water.

- Safety studies present **results consistent** with those seen with **other eyelash/eyelid cosmetic products**.
  - No evidence of adverse events reported for different prostaglandin analogues used in eye drops.

Focus of Presentation

- This presentation will not focus on the Tox Report or the IOP Assay.
  - Dr. Jennifer Ator, Ph.D., M.H.S., D.A.B.T, the author of the Tox Report, is available both days to answer any questions.
    - Board-certified Principal Toxicologist and Risk Assessor with ToxServices.
    - Ph.D. in Toxicology and M.H.S. in Environmental Health Sciences from Johns Hopkins University.
  - Craig Weiss, President of Consumer Product Testing Company which ran the IOP Assay, is available both days to answer any questions.

- This presentation will focus on the Clinical Study.
  - Longest and highest-powered clinical study conducted on any cosmetic eyelash serum containing prostaglandin analogues.
  - Important, scientifically supported conclusions that we believe meet MoCRA standards on **general safety** and **ocular irritation, eye color change and periorbital fat loss.**

- Craig Weiss will now present on his/Consumer Product Testing Company's experience, the testing methodology and the findings of the Clinical Study.

Craig Weiss / CPTC Experience

- Craig Weiss
  - **Consumer Product Testing Company** President.
  - **Independent Beauty Association** Board of Directors, Treasurer and Chairman of its Technical and Regulatory Committee.
  - **Personal Care Product Council** Member (serving on Scientific Advisory Committee).
  - **Society of Cosmetic Chemists** Member (served on Committee for Scientific Affairs).

- Consumer Product Testing Company ("CPTC")
  - Established in 1975.
  - Serves cosmetic, pharmaceutical and medical device industries with:
    - Clinical trials, microbiology, analytical chemistry, toxicology and in-vitro testing services.
  - Over 45,000 ft^2 of testing facility space.
  - Over 120 trained specialists
  - Compliant with Good Clinical Practice, Good Manufacturing Practices, Good Laboratory Practice, FDA, EPA, US Pharmacopeia Convention, ISO Accredited, and registered with the Consumer Product Safety Commission.

- CPTC **responsible** for auditing the conduct, content and reporting of the **Clinical Study**.

The Clinical Study

- **8-month** Ophthalmological In-Use Safety Evaluation on **120 female subjects** to evaluate the safety of a cosmetic lash serum containing 0.0044% IC applied once-daily.

- The Clinical Study evaluated three distinct endpoints (i) **general safety** and **ocular irritation** potential, (ii) potential for change in **ocular pigmentation**, and (iii) potential for change in **periorbital volume**.

- Protocol required both examination by a **board-certified ophthalmologist** and **endpoint analysis** at five time points (baseline, 1-month, 2-month, 4-month, and 8-month).

- Ocular pigmentation and periorbital volume endpoints were examined using **computer-assisted digital photographic analysis**.

- Data was analyzed using **standard statistical approaches** at the 95% confidence level ($p<0.05$).

Methodology (General Safety & Ocular Irritation Potential)

- At baseline, 1-month, 2-month, 4-month and 8-month intervals:

- A board-certified **ophthalmologist** examined each subject for general **eye safety and ocular irritation potential**.
  - Examined eyelids, conjunctivae, corneas, anterior chambers, and pupillary reactions, in addition to measuring visual acuity, dryness, erythema, and edema.
  - Evaluated subjects for adverse events and conformance with study protocol and criteria.

- Ophthalmologist qualifications:
  - Board-Certified, Diplomate of the American Board of Ophthalmology, Fellow of the American Academy of Ophthalmology.
  - Attending physician at St. Mary's Hospital, Overlook Hospital and Essex Specialized Surgery Institute in New Jersey.
  - B.A. in Biology from Boston University, M.S. in Biological Sciences with a concentration in Biochemistry from Drexel University, M.D. from Temple University School of Medicine.

Methodology (Ocular Pigmentation)

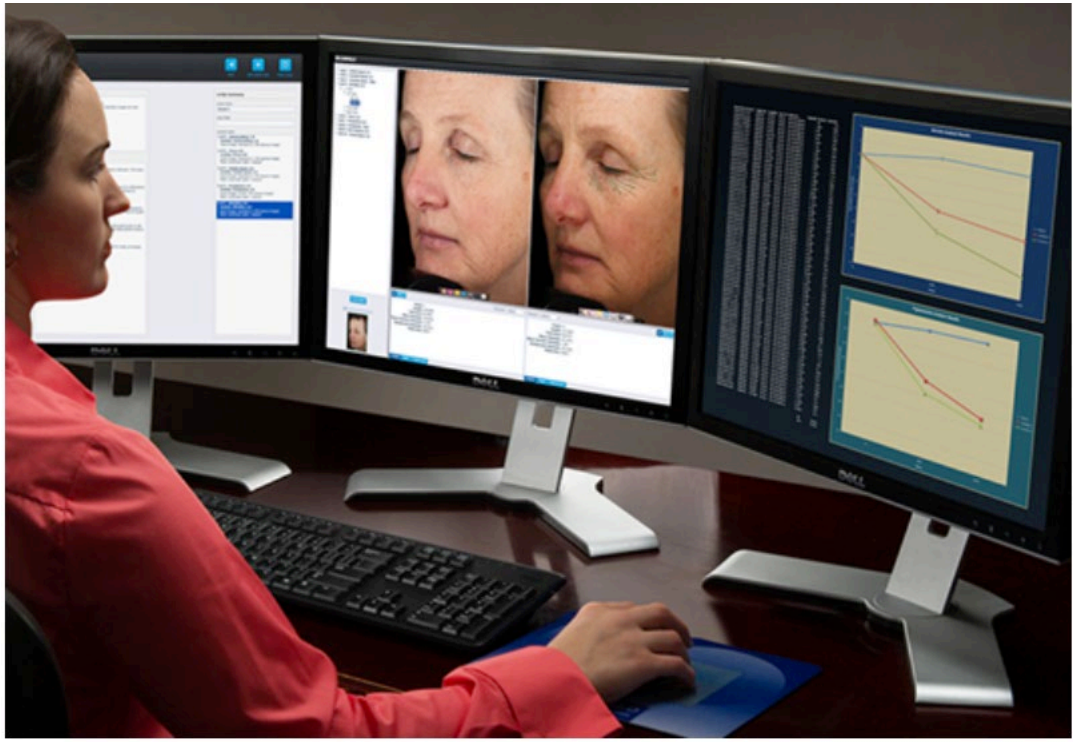
- At baseline, 1-month, 2-month, 4-month and 8-month intervals:

- A bioinstrumentation technician captured **VISIA-CR® Digital Imaging** to measure the potential for change in **ocular pigmentation**.
  - Series of standardized digital facial images, inside controlled lighting environment.

- Subjects front view captured **with eyes open** using the following lighting parameters:
  - Standard 1 – General purpose white light.
  - Standard 2 – Flat lighting.
  - Cross-polarized – filters out surface reflections for superior visualization of sub-surface detail.

Methodology (Ocular Pigmentation) (Cont'd)

- Images catalogued using **MIRROR PhotoTOOLS** software (Canfield Scientific).
- Files used for analysis using the **VAESTRO Image Analysis** Toolkit.
  - **Pixel by pixel** comparison.
  - Harnesses power of digital analysis.
- **Color analysis** performed.
  - Overall Color Change
    - $\triangle E = \sqrt{[(\triangle L^*)^2 + [(\triangle a^*)^2 + [(\triangle b^*)^2]}$
  - Individual Color Change
    - R/RGB, G/RGB and B/RGB



Methodology (Periorbital Volume)

- At baseline, 1-month, 2-month, 4-month and 8-month intervals:

- A bioinstrumentation technician captured **Aeva® 3D HE Imaging** to measure the potential for change in **periorbital volume**.
  - High resolution, 3D solution, measurement system for face topography, skin topography and body morphological changes.

- Subjects in seated position in the Visio-4D bench for stable repeatable alignment, position noted for re-positioning between measurement time points to ensure reliable and repeatable results.

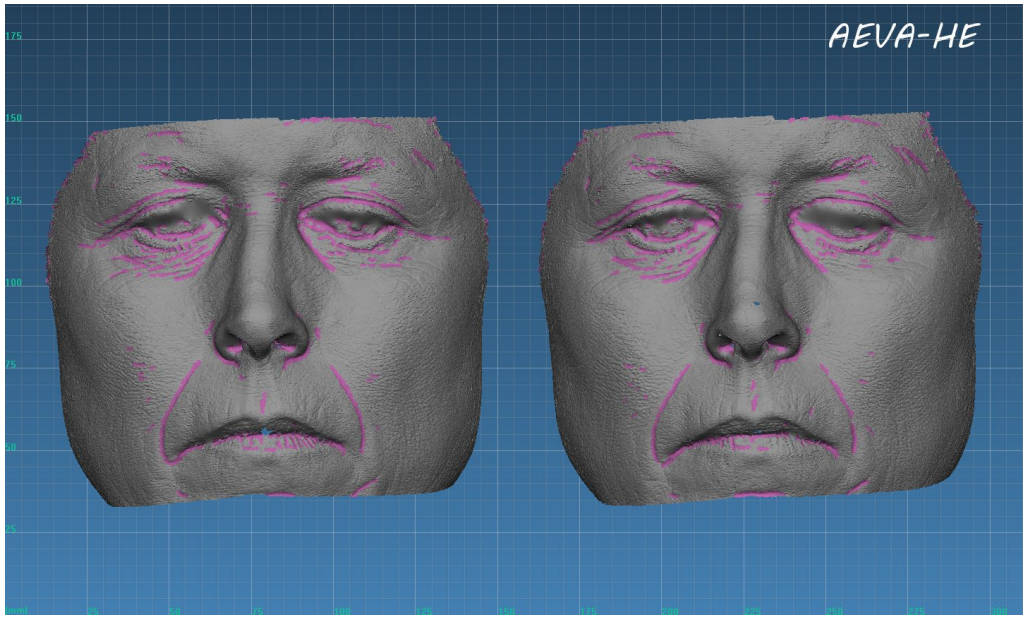
Methodology (Periorbital Volume)

- Front view Aeve-HE images were captured, using the 250 FOV Lens.

Field of View	FOV W x H x D	XY Resolution	Z Resolution	Target
Aeva-HE250	170 x 140 x 100	69 µm	5 µm	Face

- View captured the subject's **left and right orbital** region.

- These images were used to **assess** measurements in **periorbital volume**.
  - Changes measured in **mm³**.



The Clinical Study Findings

- **General Safety and Ocular Irritation Potential**: The product tested was determined to be safe for use by both contact lens and non-contact lens wearers. The lead investigator did note the product had a slight potential for transient ophthalmological irritation.
    - No visual changes in ocular pigmentation or periorbital fat volume were noted by the ophthalmologist.

- **Potential for Change in Ocular Pigmentation**: Study participants exhibited no statistically significant differences in visible eye color of the iris on the RGB scale (e.g., R/RGB (red color) G/RGB (green color), B/RGB (blue color) or L* (luminosity/brightness) from baseline after 8 months of use. In depth photography did indicate a statistically significant increase in overall color change of the iris over the length of the study (delta E) that can be attributed to changes in a*(redness /irritation) and b* (yellowness), but these changes were determined to not be clinically relevant to the issue of ocular pigmentation.

- **Potential for Change in Periorbital Volume**: There was no change in periorbital fat volume from baseline after 8 months of use.

Questions?

- We are happy to answer any questions now.

- Mr. Weiss, Dr. Ator and Mr. Abramowitz will also be available during the team meetings and on Day 2 to answer any questions from the Panel.