Clinical Ophthalmology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Evaluation of the Safety and Tolerability of Lumify Eye Illuminations Cosmetic Products

Gina Wesley[1], Melissa Morrison Toyos[2], Melinda M DiVito[3], Matthew Zirwas[4]

[1]Complete Eye Care, Medina, MN, USA; [2]Toyos Clinic, Nashville, TN, USA; [3]Medical Affairs, Bausch + Lomb, Bridgewater, NJ, USA; [4]Ohio University Heritage College of Osteopathic Medicine, Athens, OH, USA

Correspondence: Gina Wesley, Complete Eye Care, 170 Westfalen Trail, Medina, MN, 55340, USA, Tel +1 763 478 3505, Fax +1 763 478 2727, Email drwesley@cecofmedina.com

Purpose: Cosmetic products applied to the periocular area can cause skin sensitivity reactions, and manufacturers routinely test the safety and tolerability of products in development. This research was sponsored by Bausch + Lomb to evaluate three Lumify Eye Illuminations products: a lash and brow serum, a hydra-gel eye cream, and a micellar water eye makeup remover.

Methods: A cumulative irritation test (CIT) study and a repeated insult patch test (RIPT) study enrolled adult males or females with no known sensitivities to cosmetic products. Three clinical safety studies enrolled adult females with self-reported characteristics targeted by each product, which was applied in a manner consistent with expected use for 8 or 12 weeks.

Results: In CIT (n=34) and RIPT (n=201) studies, faint/minimal erythema reactions were observed in 0% to 2.9% of participants; there were no moderate or severe reactions. No safety signals were observed in participants who completed clinical safety studies for lash and brow serum (n=66 enrolled, n=55 completed [83%]), eye cream (n=61 enrolled, n=52 completed [85%]), or eye makeup remover (n=80 enrolled, n=68 completed [85%]). No clinically relevant changes in visual acuity or ophthalmologic slit-lamp examination findings were noted. No participants reported ocular sensations of burning/stinging, foreign-body sensation, or soreness. At the final clinical safety study assessment, mild cutaneous erythema (as graded by the investigator) was reported for one participant (eye cream study); no other prespecified signs of cutaneous irritation (eg, edema, dryness) were observed. A treatment-related adverse event that led to study discontinuation was experienced by one participant in the eye makeup remover study (bilateral periorbital swelling).

Conclusion: Findings from rigorously conducted irritation testing and clinical safety studies indicated that these products were safe and well tolerated. Increased availability of data regarding ocular and cutaneous safety of cosmetic products can inform consumer decision-making and eye care provider recommendations.

Keywords: cutaneous, cosmetics, irritation, periocular

Introduction

The US Food and Drug Administration (FDA) defines cosmetics as

> articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body... for cleansing, beautifying, promoting attractiveness, or altering the appearance.[1]

Of the more than 12,500 chemicals used in cosmetics, fewer than 20% have been evaluated by the Cosmetic Ingredient Review,[2] an independent organization formed with the cooperation of the FDA. Despite the wide variety of cosmetic products available, an online survey of 169 cosmetics users found that only 30% of respondents considered the ingredients when deciding which cosmetic products to purchase.[3]

Many women use cosmetics in the periocular region (eg, eyelids, eyelashes, outer-eye and under-eye skin),[4–6] and topical cosmetic products are often the first-line approach for minimizing the signs of aging and addressing common concerns (eg, crow's feet, dark circles, dry skin).[6,7] The skin of the eyelids and around the eyes is especially thin and

Received: 7 June 2024
Accepted: 26 September 2024
Published: 26 October 2024

delicate, which increases vulnerability to aging-related changes.[6,7] The potential effects of chemicals and other ingredients in skin and eye care products applied to the periocular region also must be considered.[5,7]

Skin sensitivity reactions to cosmetic products, particularly in the periocular area, can occur because of irritation from ingredients and/or sensitization from repeated applications.[4,8] Products applied to the skin appear to migrate up to 1 cm from the point of application, and cosmetics intended for periocular application often reach the meibomian glands and ocular surface.[3,9] Given that manufacturers are not required to publish or share their data for cosmetic products,[8] safety and tolerability data are rarely available to help guide selection, including for products that are applied to the periocular area.

Lumify Eye Illuminations™ (Bausch + Lomb, Bridgewater, NJ, USA) is a line of cosmetic products for use in the periocular area that includes a nourishing lash and brow serum, a hydra-gel brightening eye cream, and a micellar water eye makeup remover. These products were formulated to avoid the use of ingredients that are known to or likely to cause irritation, and we report the findings from multiple studies that were conducted to confirm their safety and tolerability. Cutaneous irritation and sensitization were evaluated using skin patch testing, and clinical studies were conducted for each product to evaluate the safety and tolerability of regular cosmetic use. The aim of this report is to summarize the results of the safety and tolerability testing for all three products to better inform clinicians about the periocular safety of these cosmetic products. In addition, performance outcomes for these products are reported briefly.

Materials and Methods

All studies reported here were conducted in accordance with US federal regulations, Good Clinical Practice guidelines, and the ethical principles set out in the Declaration of Helsinki. Study protocols were approved by an institutional review board (IRB; Clarus IRB [Schererville, IN, USA] for the irritation test studies [January 2021]; Advarra IRB [Columbia, MD, USA] for the clinical studies [March-April 2022]), and participants provided written informed consent before study procedures were initiated. Participants received monetary compensation for their time and effort in participating in these studies.

Irritation Testing

All three products were evaluated in a cumulative irritation test (CIT) study,[10] and each was also assessed in separate repeated insult patch test (RIPT) studies.[11] All irritation test studies were conducted at a single testing facility (SGS North America, Inc.; Union, NJ, USA) during October 2021 and November 2021. Adult males or females (≥18 years of age) with no known sensitivities to cosmetic products were enrolled in either the CIT or RIPT study. In all irritation test studies, a prespecified quantity of each product (~0.2 mL or 0.2 g) was applied to the participant's back using a semi-occlusive adhesive patch. For the CIT study, patches were removed approximately every 48 hours and test sites were scored, after which fresh patches were applied to the same site, for a total of six product applications within 14 days. In the RIPT induction phase, patches were removed approximately every 24 hours and scored approximately 24 hours later, after which fresh patches were applied to the same site, for a total of nine product applications within 21 days. Following a 2-week "rest period" at the completion of RIPT induction testing, a challenge patch was applied to the opposite side of the back and removed after 24 hours; this site was scored at 24, 48, 72, and 96 hours after application.

The scoring system was similar across CIT and RIPT studies. At each assessment, test sites were scored as 0 (no visible reaction), ± (faint, minimal erythema; scored as 0.5), 1 (erythema), 2 (intense erythema), 3 (intense erythema, induration, vesicles), or 4 (severe reaction with erythema, induration, vesicles, and pustules). The presence (if any) of edema, dryness, peeling, staining, and hyper- or hypopigmentation was also noted.

Clinical Safety Studies

Clinical studies evaluating safety, tolerability, and product performance were conducted separately for the lash and brow serum, eye cream, and micellar water eye makeup remover. Studies were conducted at a single testing facility (SGS Stephens, Inc.; Richardson, TX, USA) between April 2022 and October 2022. Study duration was 12 weeks for the lash and brow serum study and the eye cream study and 8 weeks for the eye makeup remover study.

Participants

All three studies enrolled adult females in good general health with no known allergies to facial skin care products, no acute or chronic ocular disease (eg, glaucoma, dry eye), and no clinically significant eye irritation on ophthalmologic examination. All women had self-reported cosmetic characteristics and/or concerns targeted by each product, and none had participated in the previous CIT or RIPT studies. Other inclusion and exclusion criteria varied somewhat by study (Table 1). Skin type was determined for each potential participant using the Fitzpatrick scale, a commonly used classification system based on the skin's pigmentation and response to unprotected sun exposure.[12]

Procedures

Each product was applied according to manufacturer guidelines, developed based on expected clinical use. For the lash and brow serum study, after face cleansing (including removal of all makeup), test material was applied once daily, in the evening, to the upper and lower lash lines, lashes, and brows. Participants were instructed not to pluck, wax, thread, shave, or trim their eyebrows for the duration of the study. For the eye cream study, after face cleansing, test material was applied around the eye area (ie, under the eyes, outer corners, eyelid areas) twice daily (morning and evening). For the eye makeup remover study, test material was used in place of the participant's normal makeup remover (if any) at least three nights per week. Participants swiped a makeup round dampened with the test material over closed eyelids and the

Table 1 Clinical Safety Studies: Inclusion and Exclusion Criteria

Study	Key inclusion criteria	Key exclusion criteria
Lash and brow serum	• Healthy women • Age: 18–54 years • Fitzpatrick skin type*: I–VI (at least n=1 per skin type) • Self-perceived damaged or sparse† eyelashes or eyebrows (eyelashes for ≥12 participants), and/or self-perceived sensitive skin around the eye area (≥12 participants), and/or regular contact lens use (≥12 participants)	• Permanent eye makeup or tattoos • Artificial eyelashes or extensions (previous 4 weeks) • Eyelash tinting/dyeing (previous 3 months) • Use of eyelash or hair growth products (previous 6 months) • Current use of a prescription ophthalmic preparation
Eye cream	• Healthy women • Age: 35–65 years • Fitzpatrick skin type*: I–VI (at least n=1 per skin type) • Self-perceived sensitive skin around the eye area (≥10 participants) • Mild to moderate‡ crow's feet wrinkles, under-eye fine lines, periocular roughness, and dullness/lack of radiance in the periocular area • Including some participants with mild to moderate‡ under-eye dark circles (≥25 participants) and/or under-eye puffiness (≥25 participants)	• Facial treatments (previous 6 months) • Cigarette smoking or vaping • Current use of prescription acne medications (oral or topical) • Use of prescription retinol products (previous 3–6 months; duration varied by product) • Use of over-the-counter retinol products (previous 4 weeks) • Current use of a prescription ophthalmic preparation
Eye makeup remover	• Healthy women • Age: 18–54 years • Fitzpatrick skin type*: I–IV • Self-perceived sensitive skin around the eye area (~20% of participants) • Regular use of eye makeup (which could include waterproof mascara) • Mild-to-moderate‡ uneven skin tone and dullness/lack of radiance in the periocular area	• Facial treatments (previous 6 months) • Permanent (eg, tattooed) eye makeup • Artificial eyelashes or extensions • Use of prescription retinol products (previous 3 to 6 months; duration varied by product) • Use of over-the-counter retinol products (previous 4 weeks) • Current use of a prescription ophthalmic preparation

Notes: *Fitzpatrick skin types: I (white, very fair; always burns easily, never tans); II (white, fair; always burns easily, tans minimally), III (cream white; burns moderately, tans gradually), IV (brown; burns minimally, always tans well), V (dark brown; rarely burns, tans profusely), VI (black; never burns, deeply pigmented). †Sparse defined as a score of 1–4 on a scale from 0–9. ‡Mild to moderate defined as a score of 3–6 on a scale from 0–9.

eye area until they were satisfied with eye makeup removal. If no eye makeup was worn that day, the test material was applied to bare skin in the eye area.

Assessments

Similar safety and tolerability assessments were conducted in all clinical studies. Ocular safety assessments included visual acuity testing, slit-lamp evaluations (performed by a board-certified ophthalmologist), and participant-rated reports of ocular sensations (ie, burning/stinging, itching, foreign-body sensation, soreness). Best-corrected visual acuity (BCVA) was assessed using a manually projected visual acuity chart (Reichert Technologies, Depew, NY). Corneal fluorescein staining was rated using a 5-point scale (0=none, 1=trace, 2=mild [barely detectable], 3=moderate [obvious staining]; 4=very strong). Cutaneous tolerability assessments were conducted for the treatment area including objective (ie, investigator-graded) ratings of erythema, edema, and dryness and subjective (ie, participant-rated) assessments of burning, stinging, itching, tightness (eye makeup remover study only), and tingling (eye makeup remover study only). For participant-rated ocular sensation items and investigator-graded and participant-rated cutaneous tolerability items, the rating scale options were 0 (none), 1 (mild), 2 (moderate), and 3 (severe), with half-point scores assigned as needed to describe the clinical condition. Adverse events (AEs) were monitored throughout each study.

In each clinical safety study, performance parameters specific to that product (eg, appearance of lash length for the lash and brow serum, crow's feet wrinkles for the eye cream, radiance/brightness of the periocular area for the eye makeup remover) were graded by the investigator at baseline and at specified intervals through the end of the study. Each performance parameter was graded using a modified Griffiths scale ranging from 0 to 9 (with half-point scores permitted).[13] For the lash and brow serum, higher scores indicated better condition (eg, more prominent appearance of lash length). For the eye cream and eye makeup remover studies, higher scores indicated worse condition (eg, more crow's feet wrinkles and dull/sallow skin appearance, respectively). In the lash and brow serum and eye cream studies, investigators were provided with reference photographs (SGS internal atlas; SGS Stephens, Inc.) illustrating each score (0 to 9) on the modified Griffiths scale for each performance parameter.

Statistical Analysis

Adverse events were summarized for the safety population of each study, which comprised all enrolled participants who used the test material at least once. The per-protocol population, which consisted of participants who completed the study with no major protocol deviations, was used for ocular safety assessments, cutaneous tolerability assessments, and product performance analyses. For clinical grading of performance parameters, improvement was defined as a change from baseline in the modified Griffiths scale score in the direction of better condition (ie, score increase in the lash and brow serum study; score decrease in the eye cream and eye makeup remover studies). The percentage of participants classified as improved at the final study assessment compared with baseline was calculated for each product performance parameter.

Results

Irritation Testing

Thirty-four participants (age range, 20–67 years; 73.5% female) completed the CIT study, and 201 participants (age range, 18–70 years; 75.6% female) completed the RIPT study. No participants discontinued study participation because of a reaction to the test material.

In the CIT study (n=34), low-level (ie, score of ± 0.5 [faint, minimal] or 1) erythema reactions were observed in one participant (2.9%) for the lash and brow serum, no participants (0%) for the eye cream, and one participant (2.9%) for the eye makeup remover (Table 2). In the RIPT study (n=201), low-level erythema reactions were observed in two participants (1.0%) during induction and no participants (0%) during challenge testing for the lash and brow serum; in two (1.0%) and one (0.5%) participants, respectively, for the eye cream; and in five (2.5%) and one (0.5%) participants, respectively, for the eye makeup remover (Table 2). There were no reactions rated as moderate or severe at any assessment; no observations of edema, peeling, staining, or hyper-/hypopigmentation; and no reported AEs in any irritation test study.

Table 2 Irritation Testing Studies: Erythema Reaction Ratings

Erythema reactions, n (%)*	CIT study (n=34)	RIPT study (n=201)	
		Induction phase	Challenge phase
Lash and brow serum			
No visible reaction	33 (97.1)	199 (99.0)	201 (100)
Faint, minimal	1 (2.9)	1 (0.5)	0 (0)
Mild	0 (0)	1 (0.5)	0 (0)
Eye cream			
No visible reaction	34 (100)	199 (99.0)	200 (99.5)
Faint, minimal	0 (0)	1 (0.5)	0 (0)
Mild	0 (0)	1 (0.5)	1 (0.5)
Eye makeup remover			
No visible reaction	33 (97.1)	196 (97.5)	200 (99.5)
Faint, minimal	0 (0)	4 (2.0)	1 (0.5)
Mild	1 (2.9)	1 (0.5)	0

Notes: *For participants with a reaction at >1 induction assessment or >1 challenge assessment, the worst reaction is reported.
Abbreviations: CIT, cumulative irritation test; RIPT, repeated insult patch test.

Clinical Safety Studies

Participants

There were 66 enrolled participants in the lash and brow serum study, 61 in the eye cream study, and 80 in the eye makeup remover study (safety population). The per-protocol population included 55 participants (83.3%) who completed the lash and brow study, 52 participants (85.2%) who completed the eye cream study, and 68 participants (85.0%) who completed the eye makeup remover study (Figure 1). The demographic characteristics of the per-protocol populations in the lash and brow serum study (n=55), eye cream study (n=52), and eye makeup remover study (n=68) are shown in Table 3.

Ocular Safety and Tolerability

At baseline, median (range) BCVA was 20/40 (20/20 to 20/400) in the lash and brow study, 20/40 (20/20 to 20/200) for the right eye and 20/30 (20/20 to 20/400) for the left eye in the eye cream study, and 20/30 (20/15 to 20/200) in the right

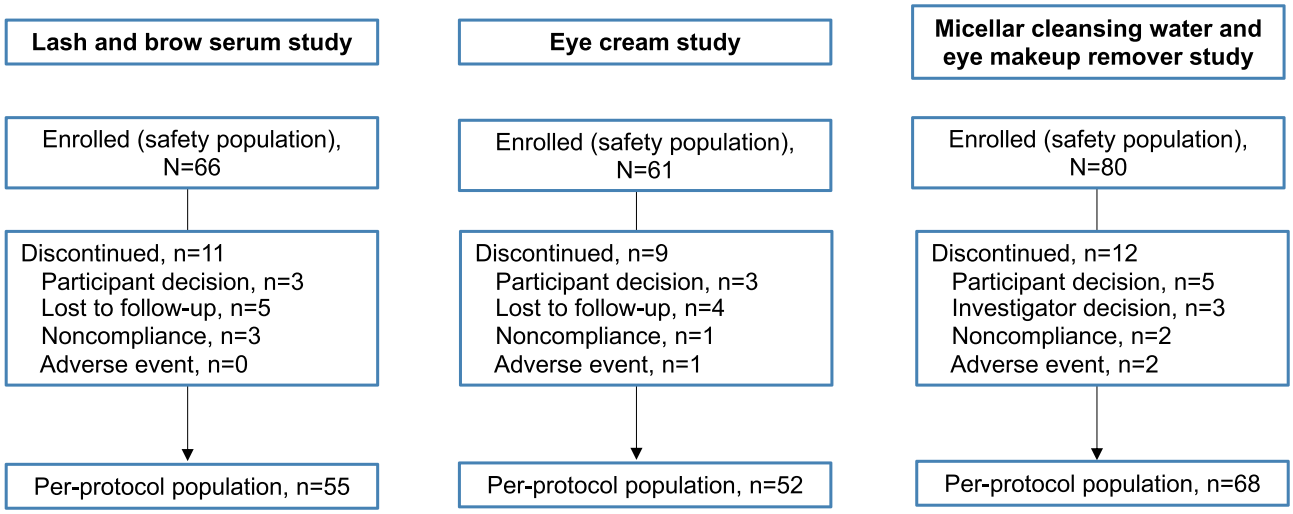

Figure 1 Participant disposition in the clinical safety studies.

Table 3 Clinical Safety Studies: Demographic Characteristics (per-Protocol Population)

	Lash and brow serum (n=55)	Eye cream (n=52)	Eye makeup remover (n=68)
Age, y			
Mean (SD)	53.9 (9.5)	56.2 (6.8)	40.8 (10.1)
Range	26–65	39–65	18–54
Fitzpatrick skin type, n (%)*			
I (white, very fair)	4 (7.3)	1 (1.9)	1 (1.5)
II (white, fair)	15 (27.3)	18 (34.6)	19 (27.9)
III (cream white)	19 (34.5)	20 (38.5)	34 (50.0)
IV (brown)	2 (3.6)	3 (5.8)	14 (20.6)
V (dark brown)	13 (23.6)	8 (15.4)	0 (0)†
VI (black)	2 (3.6)	2 (3.8)	0 (0)†
Eyewear, n (%)			
Contact lenses	8 (14.5)	3 (5.8)	14 (20.6)
Glasses	17 (30.9)	23 (44.2)	20 (29.4)
None	30 (54.5)	26 (50.0)	34 (50.0)
Eye area sensitive skin, n (%)	18 (32.7)	9 (17.3)	16 (23.5)
Damaged or sparse lashes, n (%)	42 (76.4)	—	—
Under eye dark circles, n (%)	—	36 (69.2)	—
Under eye puffiness, n (%)	—	24 (46.2)	—

Notes: *Fitzpatrick skin types: I (white, very fair; always burns easily, never tans); II (white, fair; always burns easily, tans minimally), III (cream white; burns moderately, tans gradually), IV (brown; burns minimally, always tans well), V (dark brown; rarely burns, tans profusely), VI (black; never burns, deeply pigmented). †The eye makeup remover study excluded participants with Fitzpatrick skin types V and VI.

eye and 20/35 (20/20 to 20/200) in the left eye in the eye makeup remover study. There were no substantive changes in mean BCVA in any study. The distribution of BCVA scores was generally similar at each assessment.

Across all studies, the only abnormal slit-lamp findings at follow-up visits were trace (ie, less than mild) observations of hyperemia and lacrimation. There were no clinically meaningful changes from baseline in fluorescein staining. The median score for fluorescein staining was 0.0 (none) for each eye at all assessments in all studies; the maximum value at any assessment was 1.0 (trace). At study visits, only one (eye cream study) or two (lash and brow serum study, eye makeup remover study) participants had a fluorescein staining score of 1.0 (trace). For contact lens wearers, there were few observations of lens deposits (in each study, ≤3 participants [per eye] at any assessment time point), and all were graded as mild or less than mild. Across all studies, no participants reported ocular burning/stinging, itching, foreign-body sensation, or soreness.

Cutaneous Tolerability

Findings of cutaneous irritation were uncommon, and none were rated worse than mild by the investigator or participant at any assessment. Ratings for cutaneous tolerability items at the final assessment in each study (after 8 or 12 weeks of product use) are summarized in Table 4.

Adverse Events

Adverse events led to study discontinuation of one participant in the eye cream study (COVID-19) and two participants in the eye makeup remover study (one with periorbital swelling [considered treatment-related]; one who sustained a concussion with associated eye contusion [considered not treatment-related]) (Table 5). Across studies, all AEs except one were of mild or moderate intensity and resolved by the end of the study. There was one serious AE of pneumonia

Table 4 Clinical Safety Studies: Cutaneous Irritation Ratings at the Final Assessment Time Point (per-Protocol Population)

	Investigator-graded			Participant-rated*		
	Erythema n (%)	**Edema n (%)**	**Dryness n (%)**	**Burning n (%)**	**Stinging n (%)**	**Itching n (%)**
Lash and brow serum (n=55)†						
None	54 (98.2)	55 (100)	54 (98.2)	55 (100)	55 (100)	55 (100)
0.5 (less than mild)	1 (1.8)	0 (0)	1 (1.8)	0 (0)	0 (0)	0 (0)
Mild	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Eye cream (n=52)						
None	47 (90.4)	52 (100)	50 (96.2)	52 (100)	52 (100)	52 (100)
0.5 (less than mild)	4 (7.7)	0 (0)	1 (1.9)	0 (0)	0 (0)	0 (0)
Mild	1 (1.9)	0 (0)	1 (1.9)	0 (0)	0 (0)	0 (0)
Eye makeup remover, (n=68)						
None	66 (97.1)	68 (100)	68 (100)	68 (100)	68 (100)	68 (100)
0.5 (less than mild)	2 (2.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mild	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Notes: *The eye makeup remover study also assessed tingling and tightness, which were rated as 0 (none) by all participants at all assessment timepoints. †In the lash and brow serum study, assessments were made separately for left and right eyes; results were similar between eyes and are reported here for the left eye.

Table 5 Summary of Adverse Events (Safety Population)

Adverse events, n (%)	**Lash and brow serum (n=66)**	**Eye cream (n=61)**	**Eye makeup remover (n=80)***
Any AE	11 (16.7)	5 (8.2)	5 (6.3)
Treatment-related AE	0 (0)	1 (1.6)	2 (2.5)
Discontinuation due to AE	0 (0)	1 (1.6)	2 (2.5)
Any ocular AE	2 (3.0)	1 (1.6)	4 (5.0)
Treatment-related ocular AE	0 (0)	1 (1.6)	2 (2.5)
Discontinuation due to ocular AE	0 (0)	0 (0)	2 (2.5)†
Any nonocular AE	9 (13.6)	4 (6.6)	2 (2.5)
Treatment-related nonocular AE	0 (0)	0 (0)	0 (0)
Discontinuation due to nonocular AE	0 (0)	1 (1.6)	1 (1.3)

Notes: *One participant experienced both an ocular adverse event (AE) and a nonocular AE and was discontinued from the study due to these AEs. †One participant with bilateral periorbital swelling (considered treatment-related) and one participant who sustained a concussion with associated eye contusion (considered not treatment-related).

(rated as severe and considered unrelated to the test material) in a participant in the lash and brow serum study. Few AEs were considered by the investigator to be treatment-related. One participant in the eye cream study experienced mild, treatment-related skin exfoliation of both under-eye areas. In the eye makeup remover study, one participant had moderate, treatment-related periorbital swelling (both eyes) and one participant had moderate, treatment-related eye pruritus, eye irritation, eye pain, and skin tightness in the periocular area of both eyes. There were no treatment-related AEs in the lash and brow study. Periocular AEs considered unrelated to the test material were hordeolum (two participants in the lash and brow serum study), eyelid irritation and pain (one participant in the eye makeup remover study), an arthropod bite to the outer eye area (one participant in the eye cream study), and an eye contusion (one participant in the eye makeup remover study who also experienced a concussion).

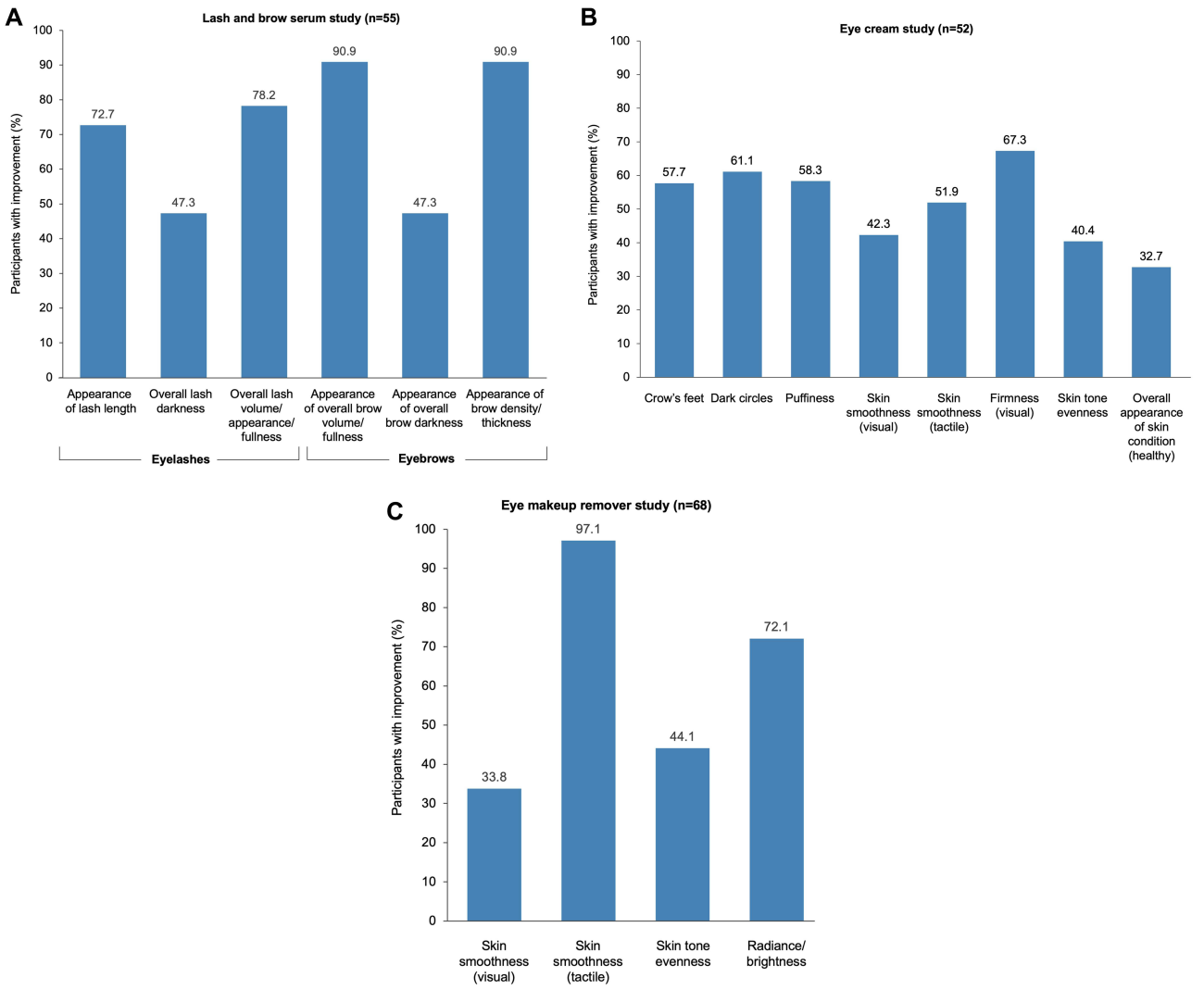

Figure 2 Percentage of participants with improvement in investigator-graded clinical parameters at the last assessment* for the (**A**) lash and brow serum study, (**B**) eye cream study, and (**C**) eye makeup remover study (per-protocol population).
Notes: * Week 12 in the lash and brow serum and eye cream studies; week 8 in the eye makeup remover study.

Product Performance

For each product performance parameter in each study, Figure 2 shows the percentage of participants with investigator gradings indicating improvement at the last study assessment (after 8 or 12 weeks of product use). In the lash and brow serum study, improvement was observed in 73% to 91% of participants for appearance of lash length, overall lash volume/appearance/fullness, appearance of overall brow volume/fullness, and appearance of brow density/thickness (Figure 2A). In the eye cream study, improvement was observed in 52% to 67% of participants for crow's feet, dark circles, puffiness, skin smoothness (tactile), and firmness (visual) (Figure 2B). In the eye makeup remover study, improvement was observed in almost all participants (97%) for skin smoothness (tactile) and in most participants (72%) for radiance/brightness (Figure 2C).

Discussion

The studies included in this report provide pertinent information regarding the ocular and cutaneous safety and tolerability of three products intended for use in the periocular area. In CIT and RIPT, faint/minimal reactions were observed in less than 3% of study participants, and there were no moderate or severe reactions. Results of clinical studies demonstrated good safety and tolerability when the products were applied to the periocular area in a manner consistent with expected use. No safety signals were observed during product use for a duration of 8 weeks (eye makeup remover)

or 12 weeks (lash and brow serum, eye cream). No clinically relevant changes in visual acuity or ophthalmologic slit-lamp examination findings were observed. No participants reported ocular sensations of burning/stinging, foreign body, or soreness. At the final study assessment, mild cutaneous erythema (as graded by the investigator) was reported for one participant (eye cream study); no other prespecified signs of cutaneous irritation (eg, edema, dryness) were observed. Across studies, only one participant experienced a treatment-related AE that led to study discontinuation (bilateral periorbital swelling in the eye makeup remover study).

The clinical safety studies also included ratings of product performance, which were tailored to evaluate changes in the eye areas to which the products were applied. Investigator ratings of product performance reflected improvements across many parameters, most notably appearance of eyelash length and volume as well as eyebrow volume and density in the lash and brow serum study; increased skin firmness and reduction in dark circles, puffiness, and crow's feet in the eye cream study; and increased skin smoothness and radiance/brightness in the eye makeup remover study.

The availability of data from this series of safety and tolerability studies is notable because there is a general lack of information in the medical literature regarding the safety of cosmetic products, even though manufacturers routinely conduct safety testing for products in development. Historically, cosmetic products and ingredients (with the exception of color additives) have not required FDA approval prior to marketing.[14] The provisions of the Modernization of Cosmetics Regulation Act of 2022 substantially expand FDA regulation of cosmetic products, including increased requirements for safety testing, which are expected to improve the availability of safety and tolerability data.[15] Consumers and health care providers must make decisions regarding the use of cosmetic products based on available safety information. Knowledge regarding the safety and tolerability profiles of cosmetic products is particularly important for people with allergies or chemical sensitivities.[8]

The primary study limitations are the relatively small sample sizes and the lack of a control group in the clinical safety studies. Sample sizes were not large enough to detect rare ocular or cutaneous AEs. Safety and tolerability profiles of these three products were not compared with those of other products targeting the same treatment areas. The dropout rate in the clinical safety studies was 15% to 17%. Since the results of similar studies are rarely published, it is unknown whether the participant completion rates observed here are comparable to those in previous research.

Many cosmetic products contain ingredients that have prompted concern regarding ocular health and safety.[4,9,16–18] Ingredients of particular concern include preservatives (eg, benzalkonium chloride, parabens), phthalates, prostaglandin analogues, and retinoids.[4,16,19] The Tear Film & Ocular Surface Society has published a comprehensive review of cosmetic ingredients that may have adverse effects (eg, allergic reaction, endocrine disruption, immunosuppression, irritation), including those that may damage the ocular surface and adnexa.[16] The products evaluated in the present studies were formulated without using ingredients known to be of concern (Table 6). The results of the safety and

Table 6 Product Ingredients

Product	Ingredients
Lash and brow serum	Aqua (water), sodium acrylates copolymer, glycerin, tetrahexyldecyl ascorbate (vitamin C), lecithin, dipotassium glycyrrhizate, 1,2-hexanediol, caprylyl glycol, sodium hyaluronate, panthenol (pro-vitamin B5), tocopheryl acetate (vitamin E), biotin (vitamin B7), disodium EDTA, myristoyl pentapeptide-17, pentylene glycol, isochrysis galbana extract, *Euphrasia officinalis* (eyebright) extract, polylysine
Eye cream	Aqua (water), butyrospermum parkii (shea) butter, niacinamide (vitamin B3), tetrahexyldecyl ascorbate (vitamin C), glycerin, squalene, sodium acrylates copolymer, alumina, dimethicone, caffeine, lecithin, 1,2-hexanediol, caprylyl glycol, synthetic fluorphlogopite, titanium dioxide, tin oxide, panthenol (pro-vitamin B5), tocopheryl acetate (vitamin E), potassium sorbate, disodium EDTA, mannitol, ergothioneine, gleditsia triacanthos seed extract, *Euphrasia officinalis* (eyebright) extract, glycyrrhiza glabra (licorice) root extract, sodium hyaluronate
Micellar water eye makeup remover	Aqua (water), isohexadecane, squalene, glycerin, niacinamide (vitamin B3), sodium ascorbyl phosphate (vitamin C), sodium hyaluronate, decyl glucoside, panthenol (pro-vitamin B5), sodium chloride, potassium chloride, sodium citrate, disodium EDTA, glycyrrhiza glabra (licorice) root extract, *Euphrasia officinalis* (eyebright) extract, citric acid, alexidine hydrochloride

tolerability studies reported herein suggest that these formulations have low potential to cause ocular or cutaneous irritation or otherwise negatively affect ocular health. It should be noted that a separate Lumify product—brimonidine ophthalmic solution 0.025% for reduction of ocular redness—has also been rigorously evaluated to confirm product safety and tolerability.[20–22] Brimonidine is a highly selective α2 adrenergic receptor agonist, and its mechanism of action (greater constrictive effect on conjunctival venules than arteries) gives these eye drops a unique safety profile, most notably a low risk of tachyphylaxis or rebound redness, relative to other ophthalmic vasoconstrictors.

Health care providers can play an important role in maintaining the ocular health of eye cosmetics users. Ophthalmologists[23] or other health care providers may be the first to observe ocular or cutaneous issues related to cosmetics use, and these clinicians can help mitigate potential harms from unsafe products. Given the importance of ocular health in the selection of cosmetic products, consumers need reliable medical and scientific sources of information. Since the vast majority of patients do not discuss cosmetic use with an eye care provider,[3] it may be necessary for health care professionals to initiate the conversation.

Conclusions

Findings from rigorously conducted irritation testing and clinical safety studies indicated that the three evaluated products—a lash and brow serum, a hydra-gel eye cream, and a micellar water eye makeup remover—were safe and well tolerated. This information on product safety may inform consumers' decisions regarding the use of cosmetics, and the FDA's enactment of the provisions of the Modernization of Cosmetics Regulation Act of 2022 should increase the availability of data regarding the safety of cosmetic products. Eye care providers, dermatologists, and other health care professionals can discuss these issues with their patients and provide reliable information on the ocular and cutaneous safety of cosmetic products.

Abbreviations

AE, adverse event; BCVA, best-corrected visual acuity; CIT, cumulative irritation test; FDA, US Food and Drug Administration; IRB, institutional review board; RIPT, repeated insult patch test.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Acknowledgments

Editorial and medical writing assistance was provided under the direction of the authors by Nancy Holland, PhD, Synchrony Medical Communications, LLC, West Chester, PA, USA, and funded by Bausch + Lomb.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

These studies were sponsored by Bausch + Lomb.

Disclosure

GW reports serving as a consultant for Alcon, Aerie, Allergan, Bausch + Lomb, BioTissue, CooperVision, Johnson & Johnson, OcuSoft, Optovue, Orasis, and Tarsus Medical; and receiving research support from Alcon, Bausch + Lomb, CooperVision, and Johnson & Johnson Vision Care.

MMT reports serving as a consultant to Bausch + Lomb, Mallinckrodt, Recordati, and Sun Pharmaceutical Industries, Inc.; serving on the speakers' bureau for Bausch + Lomb, Lumenis, Mallinckrodt, and Sun Pharmaceutical Industries, Inc.; receiving research support from Alcon, Bausch + Lomb, Dompé farmaceutici, Glaukos, Greenlight, Icon, Kala

Pharmaceuticals, Lumibird, Lumenis, Mallinckrodt, MIXTO Lasering, Ocular Technologies, Oculis, Oculus, Opternative, Recordati, RevitaLid, Shire, Sun Pharmaceutical Industries, Inc., Sylentis, and Zeiss; and receiving miscellaneous fees from MIXTO Lasering.

MMD is an employee of Bausch + Lomb.

MZ reports receiving consulting fees, investigator fees, speaker fees, clinical research grants or sponsored research, and/or honoraria from AbbVie, AnaptysBio, Arcutis Biotherapeutics, Asana BioSciences, Aseptic, Avillion, Bausch Health, Beirsdorf, Cara Therapeutics, Concert Pharmaceuticals, Dermavant Sciences, Edesa Biotech, Eli Lilly, EPI Health, Fitbit, Galderma Laboratories, Genentech/Novartis, Incyte Corporation, Janssen Pharmaceuticals, LEO Pharma, Level Ex, L'Oréal, Luum Skincare, Oculus, Peloton, Pfizer, Regeneron Pharmaceuticals/Sanofi, Sol-Gel, Trevi Therapeutics, UCB Pharma, and VYNE Therapeutics.

References

1. US Food and Drug Administration. Cosmetics & U.S. law. Department of Health and Human Services. [Updated February 25, 2022]. Available from: https://www.fda.gov/cosmetics/cosmetics-laws-regulations/cosmetics-us-law. Accessed September 11, 2023.
2. Wang J, Liu Y, Kam WR, Li Y, Sullivan DA. Toxicity of the cosmetic preservatives parabens, phenoxyethanol and chlorphenesin on human meibomian gland epithelial cells. *Exp Eye Res*. 2020;196:108057. doi:10.1016/j.exer.2020.108057
3. O'Dell LE, Sullivan AG, Periman LM. Beauty does not have to hurt. *Adv Ocul Care*. 2016;7:42–47.
4. Ng A, Evans K, North R, Purslow C. Eye cosmetic usage and associated ocular comfort. *Ophthalmic Physiol Opt*. 2012;32(6):501–507. doi:10.1111/j.1475-1313.2012.00944.x
5. Ng A, Evans K, North RV, Jones L, Purslow C. Impact of eye cosmetics on the eye, adnexa, and ocular surface. *Eye Contact Lens*. 2016;42 (4):211–220. doi:10.1097/ICL.0000000000000181
6. Vrcek I, Ozgur O, Nakra T. Infraorbital dark circles: a review of the pathogenesis, evaluation and treatment. *J Cutan Aesthet Surg*. 2016;9(2):65–72. doi:10.4103/0974-2077.184046
7. Pilkington SJ, Belden S, Miller RA. The tricky tear trough: a review of topical cosmeceuticals for periorbital skin rejuvenation. *J Clin Aesthet Dermatol*. 2015;8(9):39–47.
8. Norris MR, Bielory L. Cosmetics and ocular allergy. *Curr Opin Allergy Clin Immunol*. 2018;18(5):404–410. doi:10.1097/ACI.0000000000000474
9. Wang MT, Craig JP. Investigating the effect of eye cosmetics on the tear film: current insights. *Clin Optom*. 2018;10:33–40. doi:10.2147/OPTO.S150926
10. Do LHD, Maibach H. The 21-day cumulative irritation assay in man: a half-century summary and re-evaluation. *Cutan Ocul Toxicol*. 2021;40 (2):61–65. doi:10.1080/15569527.2021.1887885
11. McNamee PM, Api AM, Basketter DA, et al. A review of critical factors in the conduct and interpretation of the human repeat insult patch test. *Regul Toxicol Pharmacol*. 2008;52(1):24–34. doi:10.1016/j.yrtph.2007.10.019
12. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. *Arch Dermatol*. 1988;124(6):869–871. doi:10.1001/archderm.124.6.869
13. Griffiths CE, Wang TS, Hamilton TA, Voorhees JJ, Ellis CN. A photonumeric scale for the assessment of cutaneous photodamage. *Arch Dermatol*. 1992;128(3):347–351. doi:10.1001/archderm.1992.01680130061006
14. US Food and Drug Administration. Is it a cosmetic, a drug, or both? (Or is it soap?). Department of Health and Human Services. [Updated February 25, 2022]. Available from: https://www.fda.gov/cosmetics/cosmetics-laws-regulations/it-cosmetic-drug-or-both-or-it-soap. Accessed March 22, 2023.
15. Bergeson, Campbell PC Congress enacts Modernization of Cosmetics Regulation Act of 2022, significantly strengthening regulation of cosmetics. [Updated September 11, 2023]. Updated https://www.natlawreview.com/article/congress-enacts-modernization-cosmetics-regulation-act-2022-significantly. Accessed September 5, 2023.
16. Sullivan DA, da Costa AX, Del Duca E, et al. TFOS lifestyle: impact of cosmetics on the ocular surface. *Ocul Surf*. 2023;29:77–130. doi:10.1016/j.jtos.2023.04.005
17. Yazdani M, Elgstøen KBP, Utheim TP. Eye make-up products and dry eye disease: a mini review. *Curr Eye Res*. 2022;47(1):1–11. doi:10.1080/02713683.2021.1966476
18. Tang K, Lu SY, Ma DL, et al. A review on common ingredients of periocular cosmetics and their hazards. *Curr Org Chem*. 2015;19(1):30–38. doi:10.2174/1385272819666141107225726
19. Ding J, Kam WR, Dieckow J, Sullivan DA. The influence of 13-cis retinoic acid on human meibomian gland epithelial cells. *Invest Ophthalmol Vis Sci*. 2013;54(6):4341–4350. doi:10.1167/iovs.13-11863
20. McLaurin E, Cavet ME, Gomes PJ, Ciolino JB. Brimonidine ophthalmic solution 0.025% for reduction of ocular redness: a randomized clinical trial. *Optom Vis Sci*. 2018;95(3):264–271. doi:10.1097/OPX.0000000000001182
21. Torkildsen GL, Sanfilippo CM, DeCory HH, Gomes PJ. Evaluation of efficacy and safety of brimonidine tartrate ophthalmic solution, 0.025% for treatment of ocular redness. *Curr Eye Res*. 2018;43(1):43–51. doi:10.1080/02713683.2017.1381269
22. Ackerman SL, Torkildsen GL, McLaurin E, Vittitow JL. Low-dose brimonidine for relief of ocular redness: integrated analysis of four clinical trials. *Clin Exp Optom*. 2019;102(2):131–139. doi:10.1111/cxo.12846
23. Janetos TM, Thyparampil P. Ocular cosmetics: public safety problem or harmless products? *Ophthalmic Plast Reconstr Surg*. 2019;35(3):294–295. doi:10.1097/IOP.0000000000001337