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Department of Health and Human Services

Food and Drug Administration

5630 Fishers Ln. Rm. 1061

Rockville, MD 20852

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### Citizen Petition

The undersigned, Christine C. Oddo dba/Madison Company, submits this Citizen Petition under section 505 of the Federal Food, Drug and Cosmetic Act and 21 CFR §10.30 to request the Agency to permit the marketing of active ingredient: Tetrahydrozoline Hydrochloride 0.01 to 0.05% in consumer cosmetic leave-on topical skin gels, skin creams, and skin lotions for external face and body formula applications. The basis for this petition is that Tetrahydrozoline Hydrochloride is a Category 1 drug active ingredient deemed generally recognized as safe and effective for over-the-counter use.

Currently Tetrahydrozoline Hydrochloride is solely classified within 21 CFR 349 and 369 Ophthalmic Drug Products for Over-the-Counter Human Use as a vasoconstrictor for relief of eye redness. With interim marketing approval for use in cosmetic topical skin gels, creams and lotions, it would thereby include this active ingredient in 21 CFR 310, 347 and 352 Skin Protectant Drug Products for Over-the-Counter Human Use.

### Action Requested

This petition requests that during the process to include Tetrahydrozoline Hydrochloride in to 21 CFR 310, 347 and 352 Skin Protectant, that the Agency issue a notice of enforcement policy allowing the interim marketing of this ingredient before a Final Amendment is published.

### Statement of Grounds

There are several significant grounds for this petition and the prudent logic that it will receive a positive ruling. These grounds include the long-standing and extensive use of the ingredient, the

immense records of safety and efficacy of the ingredient, efficient rewards utilizing the Agency's resources in contributing to public health and wellness and extensive consumer market demand. See Table 1 for input on the transference of current labelling language for ophthalmic use into skin protectant use.

#### I. Use of Tetrahydrozoline Hydrochloride and Safety and Efficacy Record

This drug ingredient is proven safe and effective currently used as an ophthalmic vasoconstrictor. The user typically experiences a really high level of gratification as the ingredient offers very fast positive results for the relief of redness due to minor irritation of the eye. The eye is one of the most sensitive parts of the external human body and readily absorbs the redness relieving product. It appears consistent that a drug approved and proven safe and effective for the eye would be generally considered safe and effective for topical cosmetic skin application. In 21 CFR 349 and 369 the Agency thoroughly reviewed safety and efficacy issues and deemed Tetrahydrozoline Hydrochloride as safe and effective for the use of relief of redness due to minor irritation. For the safety issue of children swallowing the material, the label warning can adopt 21 CFR 201, 310 and 352 Sunscreen Drug Products for Over-the-Counter Use requirements.

#### II. Efficient Use of Agency Resources for Public Health and Wellness

This petition requests that Tetrahydrozoline Hydrochloride be able to be used so it can provide the same relief for topical skin redness from minor irritation just as it is currently allowed for eyes. With the Agency's extensive knowledge of this drug and current regulations supporting it, translating these same parameters from 21 CFR 349 and 369 Ophthalmic Drug Products to 21 CFR 310, 347 and 352 Skin Protectant would be an efficient utilization of Agency resources for maximum public benefit.

#### Skin Protectant 21 CFR 310, 347 and 352

Definition: A drug product that temporarily protects injured or exposed skin or mucous membrane surfaces from harmful or annoying stimuli, and may help provide relief to such surfaces.

Like eyes, skin presents visible redness when it is considered injured from annoying stimuli.

There are many annoying stimuli in common everyday life that cause visible redness.

Skin redness may occur from the many common everyday annoying stimuli such as the work place HVAC, travel, plant matter, pollutants, facial regimens such as washing, applying cosmetics, and shaving, pets, cleansers, and retail environments- these are all legitimate daily skin irritants that can cause mild temporary redness and for which the consumer would welcome an additional option to offer temporary relief from the condition. In addition “red blotchiness of patches of ruddiness on facial skin are fairly common dermatological complaints, and may result from post-acne inflammation, irritation, aging, UV damage or rosacea.”<sup>1</sup> Skin and eyes exhibit common redness responses to the sources and causes of outside irritants.

#### Current Product Marketplace Offerings Summary by Regulatory Category

##### a) Cosmetic

There is an extreme variety of cosmetic products with cosmetic claims currently on the market. The consumer mostly recognizes marketing claim such as “calming”, “redness reducer”, and “redness relief”. Ingredients fall in to the main categories of plants, oils and minerals such as: aloe, cucumber, chamomile, shea butter, almond oil, jojoba oil, comfrey, white tea leaves, and zinc, copper and magnesium. These ingredients can be found in leading mass and prestige brands such as Clinique, L’Oreal, Olay, Bare Escentuals, and Murad.

##### b) OTC

Colloidal oatmeal, allantoin, dimethicone, glycerin are the most commonly used and consumer recognized as ingredients that are associated with cosmetically elegant daily facial beauty regimen products. These ingredients can be found in leading consumer brands -such as Aveeno, and Eucerin. Product searches reveal that at an OTC level concentrate; there are few consumer choices in this category.

##### c) Prescription

The Agency recently granted Galderma Laboratories LLP approval for Brimonidine the active ingredient marketed as Mirvaso<sup>®</sup> for the treatment of skin redness associated with Rosacea. “Mirvaso<sup>®</sup> is a topical gel that may work by constricting the dilated facial blood vessels to reduce the redness of rosacea. Mirvaso<sup>®</sup> should be applied in a pea-sized amount, once daily to each of the five regions of the face: the forehead, chin, nose and each cheek.”<sup>4</sup> Mirvaso<sup>®</sup> (brimonidine) topical gel, 0.33% is available by prescription is indicated for the topical treatment of persistent (nontransient) facial erythema of rosacea and is not for children, it is only allowed for adults 18 years of age or older.<sup>5</sup>

Background: Brimonidine, now approved for topical skin application also began as a prescription eye drug. For ophthalmic uses, it is currently marketed as Alphagan<sup>®</sup> P (brimonidine tartrate ophthalmic solution), with a dosage range of 0.1% or 0.15%<sup>8</sup> and is an alpha-adrenergic and is indicated for the reduction of elevated intraocular pressure for patients with open-angle glaucoma or ocular hypertension.

In consideration of this review this market review, it can be suggested that currently, there is not readily available an OTC drug remedy for the condition of mild skin redness at the equivalent marketability, safety and effectiveness levels as Tetrahydrozoline Hydrochloride.

### III. History, Pursuit and the Marketplace Importance of Even Skin Tone

The studies and reference material on the desire for even skin tone is immense. The pursuit is noted amongst and across gender, age and ethnicity. It is also rich in history as recordings in very early cultures indicate that even skin tone was the most favored and preferred presentation of one's image, status and health. "Asian countries have long histories of utilizing white skin as a key criterion of personal beauty. In Korea, flawless skin like white jade and an absence of freckles and scars have been preferred since the first dynasty in Korean history (the Gojoseon Era, 2333-108 BCE)."<sup>2</sup> Opinions also exist as to the level of prejudice there is associated with the qualities and pursuit of even skin tone. The desire to pursue this symbolic imagery of youth, wellness and wealth is recorded in our oldest human cultures and perpetuated by the same today. One can disagree with the negative social impacts of this pursuit, but the market's desire for even skin tone shows no indication of abatement.

Additional notable extractions from credible sources are available as noted below. In addition, a personal testimony is included at the end of this section.

- "Trends in makeup have been shifting more towards the natural no-make up look. As such, having an even skin tone takes on an ever greater prominence. "Some beauty executives say the new look reflects greater interest in skin care and a broader cultural focus on wellness. Not many women who are at spin class at dawn and sipping green juice for breakfast want to apply a full face of makeup"<sup>4</sup>

- In 2013, the word Selfie was the word of the year.<sup>9</sup> Our social media communication is a ubiquitous form of communication that is largely driven by imagery. “Young consumers continuing preoccupation with image has brought about more tailored offerings, with a rise in specific solution-based products that consumers can relate to. Examples include hyperpigmentation, evening skin tone, scalp health and anti-ageing for hair, among others.”<sup>10</sup>
- “New psycho-social research is demonstrating how vital skin tone is to age and beauty perceptions, and scientists are gaining new insights into why skin’s luminosity and uniformity of tone tends to degenerate with age. Scientists and dermatologists are beginning to recognize that repairing tone problems is as important as repairing texture problems, and are increasingly able to offer women better and more accessible solutions to achieve luminous and more even skin tone.”<sup>1</sup>
- “In a study presented at the 2007 American Academy of Dermatology annual meeting and published in the November 2006 issue of *Evolution and Human Behavior*, P&G Beauty researchers established the degree to which skin tone affects perception of age, healthiness and youth. Estimated biological age ranged from 17 to 37 years, demonstrating that uneven skin tone *alone* can account for up to 20 years of age perception, *independent of facial form and topography*.”<sup>11</sup>
- “In the case of both color and texture, contrast seems to be the key – or more precisely, the lack of contrast. That’s because the human eye is drawn to edges created by contrast. Human skin is not a solid opaque structure, rather it has depth and layers, and its appearance is determined by how much light is ultimately reflected back to the eyes. Facial skin normally allows more than 90 percent of light to penetrate its surface. White light passing through the skin’s transparent surface is scattered back toward the surface by dermal collagen, which acts essentially as a mirror within the skin.”<sup>1</sup>
- “The wide range of skin colors – from the deepest chocolate brown of Africa’s Ivory Coast to the warm olives of the Mediterranean to the pale fairness of Scandinavia – is paralleled by a similarly wide array of cultural beliefs that define “ideal skin tone” in various geographic regions. Western

women may desire the healthy glow of sun-kissed skin, while Asian cultures value paleness, even going to great lengths to lighten skin. Yet despite these seemingly contradictory goals, even skin-tone is one common quality that defines beautiful desirable skin all over the world”<sup>3</sup>

- Personal testimony and self-reported results: the author of this petition is a highly experienced professional in the beauty industry. Industry employment positions include sales and marketing as well as product development for the primary brand and within a contract manufacturer. Approximately 15 years ago, adult acne with millia set in. Extreme red bumps that seemingly never healed were constant and were highly professionally and socially embarrassing, created a lot of sadness and also frustration. Intense pre-occupation with a self-perceived debilitating condition causes anxiety and reduces productivity. Then, upon pure accident, it was noticed that when an eye redness reliever product inadvertently ran down my face after use, there was a white streak left behind. It gave the idea to apply redness reliever to the red area on the face. Without question, it worked incredibly. Since redness reliever product is in liquid form, it was not possible to keep it in one place on the face to soak in and a lot of product was therefore wasted. As a result, I began to mix redness reliever product with a variety of cosmetic skin care products. This application gave the needed redness relieving results to avoid embarrassment by keeping the redness more under control. It also provided the freedom to go without make up on occasion and to also wear far less for cover up products and use less drying acne control medications. Unquestionably in the approximately 15 years of this home practice, I can self-report that there has not been one indication of irritation after use. And this accounts for direct application of the redness reliever as well as using redness reliever mixed in to a cosmetic product.

#### Labeling, Concentration and Packaging

Within the period of approval for interim marketing of Tetrahydrozoline Hydrochloride in 21 CFR 347 Skin Protectant Drug Products, the required elements of identity, indications, use and warning, as well, as any other labeling requirements, would directly emulate those as derived from 21 CFR 349, Ophthalmic Drug Products. The language emulating Ophthalmic use would be sensibly restated as appropriate for the Skin Protectant application. Petitioner appeals that the

Agency recognize that the ease and appropriateness in which this language transfers is another indication of the logic for a positive finding.

Table 1 showing original language for Ophthalmic use and the emulated language for Skin Protection use.

Language	Ophthalmic <sup>6</sup>	Proposed Skin Protectant
Identity	Redness reliever	Redness reliever
Indications	Relieves redness of the eye due to minor eye irritations	Relieves redness of the skin due to minor skin irritations
Use	Instill 1 to 2 drops in affected eye(s) up to four times daily	For spot treatment: place a small pea sized amount of product on red area and allow to sit for up to 20 minutes. Rub in remainder of product or wipe off*apply cosmetics or other skin products as usual
Warning	21 CFR 349.75 (c)	21 CFR 201, 310 and 352 for Sunscreen: For external use only*do not use on damaged or broken skin*stop use and ask a doctor if rash occurs*keep out of eyes. Rinse with water to remove*keep out of reach of children. If swallowed, get medical help or contact a poison control center right away.

### Concentration and Packaging

As in the language guidelines and requirements, the concentration and combination parameters for the Skin Protection category during the interim marketing period will also emulate the Ophthalmologic category.

- Tetrahydrozoline permitted concentrate 0.01 to 0.05%<sup>6</sup>
- Child Protective Packaging as specified<sup>6</sup>

### Environmental Impact

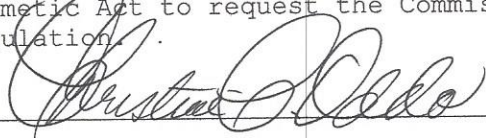
This petition qualifies for a categorical exemption from the requirements of submission of an environmental assess within 21 CFR §25.

### Economic Impact

In accordance with 21 CFR 10.30(b), information on the economic impact of the petition will be provided upon request.

### Certification

The undersigned submits this petition under the Federal Food, Drug and Cosmetic Act to request the Commissioner of Food and Drugs to amend a regulation.



\_\_\_\_\_  
(Signature)

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