CRIZAL® PREVENCIA™ LENSES

Frequently Asked Questions

FAQ

Crizal® PREVENCIA™

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I. Eye Health

1. What is AMD?

- AMD (Age-related Macular Degeneration) is a degenerative disease of the retina. It occurs when the very sensitive cells of the macula, that is the visual center of the retina, are damaged.
- People suffering from this disease cannot use the very center of their field of vision: the area that is essential to read, drive, watch television, and recognize faces.

2. What is the difference between dry and wet AMD?

- "Wet" AMD causes the most serious vision loss (10 to 20% of total AMD cases). In this form of the disease, tiny unhealthy blood vessels grow under the retina. These blood vessels often break and leak, causing loss of vision. It can lead to loss of vision of central vision. Peripheral vision usually remains intact.
- The most common form of AMD is "dry" (prevalence 90%-80%) and is characterized by progressive disappearance of macular visual cells. This AMD form usually progresses more slowly and can cause profound vision loss.

3. What are the main signs of AMD?

The main signs that a patient can have AMD are[1] [2] [3] [4]:

- A decrease in visual acuity
- One or more scotomas (dark spots seen by the patient)
- A decrease in the perception of contrasts
- Discomfort in night vision
- Straight lines are seen wavy or curvy (Metamorphopsia): the Amsler test consists of a grid of evenly spaced horizontal and vertical lines.

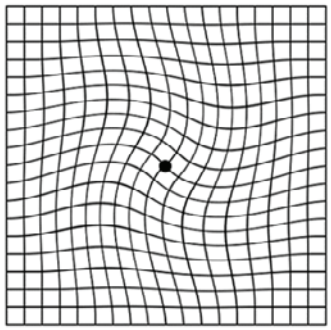

Image Courtesy: National Eye Institute, National Institutes of Health

[1] http://www.has-sante.fr/portail/upload/docs/application/pdf/2012-09/09r09_synth_dmla_fiche_diagnostique.pdf
[2] www.nei.nih.gov
[3] www.aoa.org/macular-degeneration.xml
[4] www.amd.org

A small dot is located in the centre of the grid for the person taking the test to focus on. While staring at the dot, the person will look for wavy lines and missing areas of the grid.

4. How do you know that someone is predisposed to AMD? Are there ways to test it?

- **Genetic predisposition:**

  In 2005, a strong genetic link between AMD and variants of the complement factor H (CFH) gene on chromosome 1q31 was discovered. The Y402H genetic variant of CFH gene is commonly associated with AMD. There are many genetic factors linked to the development of AMD.

Genetic tests:

Several genetic tests are currently available and/or under development.

Test	Website	Sample	Comments
Macula Risk® Gx	www.maculariskcom	Cheek swab	Two main tests in USA
RetnaGene™ AMD	http://www.sequenomcmm.com/amd/	Cheek swab or blood	
ARUP Laboratories	http://www.aruplab.com/	Blood	
deCode Complete Scan	http://www.decode.com/	Cheek swab	MD part of test to check for 50 genetic predisposition to other illness

Example: Macula Risk is one of the commercially available genetic tests that measures inheritable risk factors for AMD. When its results are combined with other risk factors (such as smoking), Macula Risk can help predict an individual's prognosis for progression towards the more advanced stages of macular degeneration.[5]

The test only requires a simple in-office cheek swab, which is sent directly to the genetic lab. A report is faxed back to the prescribing doctor, which is followed by a written report in the mail a few weeks later. The report includes the test results as well as recommended genetic support for the patients.

The family history in terms of AMD is therefore also a question that Eyecare Professionals may ask to evaluate the patients, to assess the need for retinal examination.

[5] Seddon JM, Reynolds R, Maller J, et al. Prediction model for prevalence and incidence of advanced age-related n=macular degeneration based on genetic, demographic, and environmental variables. Invest Ophthalmol Vis Sci. 2009 May; 50(5):2044-53.

- **Retinal tests:**

  To look for first signs of AMD, ophthalmologists & optometrists perform different kinds of retinal examinations.

  - Optical Coherence Tomography (OCT): OCT uses a retinal camera, for back of the eye examination using ophthalmoscope. In the early stages, ECPs look for deposits of cellular debris, called drusens, which accumulate underneath retinal cells called RPE (retinal pigmented epithelium).[6] [7]

  - Digital Fundus Photograph: A fundus camera is used to take pictures of the back of the eye to identify any abnormalities. For example if doctors suspect that abnormal blood vessels are growing, such as in the wet form of AMD, the fundus photograph may be used to shoot a rapid sequence of images showing blood flow in the eye. These high-contrast still frames or movies allow doctors to visualize and track the growth of abnormal blood vessels.

5. What other factors influence the development of AMD?

- Age
- Genetic
- Light exposure
- Smoking (risk could increase by 4 times)
- Obesity (risk could double)
- Lack of antioxidant in the daily diet

[6] Fletcher AE, Bentham GC, Agnew M, Young IS, Augood C, et al. (2008) Sunlight exposure, antioxidants, and age-related macular degeneration. Arch Ophthalmol 126: 1396-1403.

[7] Butt AL, Lee ET, Klein R, Russell D, Ogola G, et al. (2011) Prevalence and risks factors of age-related macular degeneration in Oklahoma Indians: the Vision Keepers Study. Ophthalmology 118: 1380-1385.

6. What and where is the macula?

The macula is an oval-shaped highly pigmented yellow spot near the center of the retina of the human eye. It has a diameter of around 5.5 mm (about 5% of retinal size). In its center is the fovea 1.5mm, a small pit that contains the largest concentration of cone cells in the eye and is responsible for central, high resolution vision.

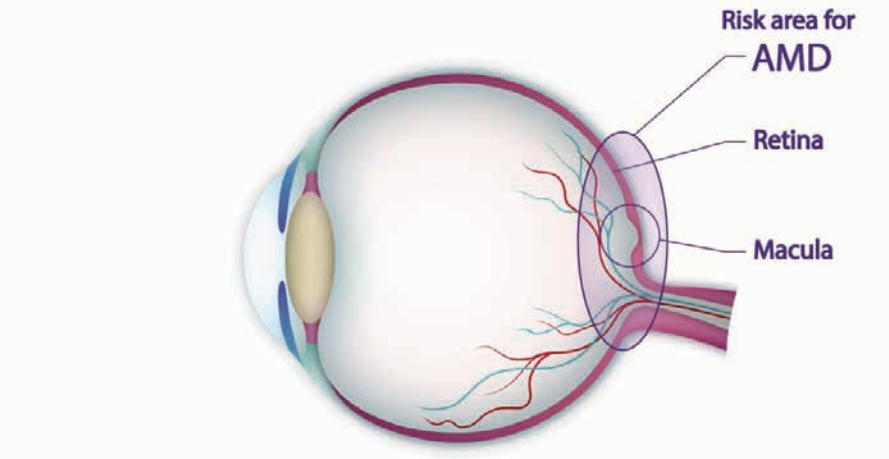

Image for illustration purposes only

7. Why is protecting the macula so important?

The macula is small but very important. It makes up only 5% of the surface of the retina; however it transmits up to 90% of the visual information processed by the brain. This is explained by its location that is in the optical axis of the eye. It is in this area that the image of the object viewed is formed. Its richness in visual cells allows it to perceive the fine details and colors.

II. Photobiology & the Discovery

1. What is the IDV (Institut De La Vision)?

Paris Vision Institute (IDV) is considered one of Europe's foremost integrated research centers on eye diseases. Researchers, medical doctors and industry players all work together on the discovery and evaluation of new therapies and new preventive solutions, as well as compensatory technologies for vision impairment.

Around fifteen different research teams and more than 200 researchers are working on various different vision-related problems. They have access to the very latest analysis, exploration and retina imaging devices and techniques.

2. What research did Essilor conduct in collaboration with Paris Vision Institute?

Essilor partnered with Paris Vision Institute to identify the wavelengths in the visible light spectrum most harmful to retinal cells. The main aim was to calculate the relative quantity of light reaching the retina in each wavelength. The toxicity of these relative intensities was measured using an AMD cell model (with porcine/swine retinal cells). Optics specialists from Essilor took part in the project to help design optical devices to calculate retinal light intensities and to manipulate concepts involving light, while researchers from the Paris Vision Institute brought their knowledge of vision and their know-how in experimental biology as applied to the retina.

An illumination device was produced, that helped convey light on very restricted, narrow wavelengths—and the visible light spectrum was split into 10-nanometer bands. Each band was guided by an optic fiber toward a cell incubator. This allowed helped to split the visible light spectrum and precisely control the degree of illumination for each wavelength. For each 10 nm band of light, intensities of illumination in proportion to those of the solar spectrum were produced.

With this experiment, Essilor and Paris Vision Institute were able to identify the specific range of visible light that is most harmful to retinal cells – **415 nm to 455 nm**. This **40 nm band of visible** light most harmful to retinal cells is called **Blue-Violet** light.

3. Why is it important to identify the specific band of blue light that is most harmful?

Light can be both harmful and beneficial to the eyes and overall health. Blue light, also known as High Energy Visible (HEV) light ranges from 380 nm to 500 nm. There are certain wavelengths of blue light that are beneficial to our eyes and overall well-being. Blocking all blue light deprives our body from this beneficial blue light. Thus, it is very important to identify the specific band of blue light that is most harmful, so that a more targeted solution is developed.

4. What is Blue-Turquoise light?

The range of visible light from **465 nm to 495 nm** is called **Blue-Turquoise** light. Blue-Turquoise light is beneficial for vision and everyday health. It aids various physiological functions like the sleep/wake cycle, cognitive performance, memory, pupillary constriction reflex etc.

5. What is the role of Blue-Turquoise light on the pupillary reflex?

Several studies have already demonstrated that pupil constriction is wavelength-dependent. It is maximum at a light excitation centered around 480 nm.

More recently, a Japanese team showed that, filters blocking light at around 470nm could disrupt the sustained phase of pupil constriction after a light excitation[8]. In other words, filters rejecting wavelengths at around 480nm could induce pupil dilation and consequently increase the energetic power of non-filtered wavelengths reaching the retina[9], particularly the harmful Blue wavelengths.

6. Why were porcine/swine retinal cells used in the experiments?

The RPE cells used in the experiments came from swine retinas. Swine retinas are biologically very close to human retinas.

Swine are known as an established model in human health because of their anatomical and physiological characteristics comparable to humans. For the eye, size and cone density are very similar. Hence swine retinal cells were used in the experiments.

7. What is the role of Blue-Violet light in AMD onset?

Lipofuscin is a fine granular pigment found in the retina. It is phototoxic and the RPE (Retinal Pigment Epithelium) cells slowly accumulate lipfuscin as we age. Lipofuscin is a heterogeneous mixture of “metabolic waste” that forms with age; it cannot be cleared from the retina. It can

[8] H. Ishikawa, A. Onodera, K. Asakawa, S. Nakadomari, K. Shimizu, Jpn J Ophthalmol, 2012
[9] F. Behar-Cohen et al., Prog Retin Eye Res 30, 239, 2011

appear in the form of drusens. An increased accumulation of lipofuscin is a risk factor for developing AMD.

Lipofuscin is commonly known as “age pigment” or even “age marker”

Exposure to Blue –Violet light can on the increase the production of lipofuscin which in turn can be lead to age-related macular degeneration (AMD).

8. What is drusen?

Drusen are yellow deposits under the retina. Often found in people over age 60, drusen can be seen by an eye care professional during an eye exam in which the pupils are dilated. Drusen by themselves do not usually cause vision loss, but an increase in their size and/or number increases a person's risk of developing advanced AMD, which can cause serious vision loss.

9. Does Blue-Violet light both impact dry and wet AMD?

In both cases, **Blue-violet light contributes to the accumulation of lipofuscin** granules in retinal pigment epithelium (RPE) cells.

Next, it has been suggested that **lipofuscin accumulation in RPE contributes to the formation and accumulation of drusens in AMD[10] [11].**

Besides, **drusens** accumulate underneath RPE **in the two AMD** forms (2 types of drusens) and already in the early stages of the disease[12].

- Blue-violet light may have a harmful impact on the 2 AMD forms.
- With the disease progression, two types of drusen are identified:
  - A first type, said “hard” is small, with sharp edges. It is associated with dry AMD (80 to 90% of patients)
  - A second type, known as soft or fluffy, is larger and has indistinct edges. It is associated with wet AMD. In this case, neovascularisation can be amplified by the large presence of oxygen in the retina (which also promotes oxidative stress).

[10] Delori FC, Goger DG, Dorey CK (2001) Age-related accumulation and spectral distribution of lipofuscin in RPE of normal subjects. Invest Ophthalmol Vis Sci. 42:1855-66.
[11] Weiter JJ, Delori FC, Wing GL et al (1985) Relationship of senile macular degeneration to ocular pigmentation. Am J Ophthalmol. 99:185-7
[12] Curcio, 1999

10. Where is Blue-Violet light present?

Blue-Violet light is present both outdoors and indoors.

- **Outdoors:** The sun emits Blue-Violet light all year long, in all weather conditions.
- **Indoors:** Blue-Violet light is emitted by many indoor sources of light such as LED lamps, compact fluorescent light bulbs (CFLs), etc. Blue-Violet light is also present in many modern digital devices like computer screens, tablets, many smartphones etc.

The images below show the intensities of visible light emission at various wavelengths, by the sun, modern lighting and devices. It is clear from the images that all these modern devices and lighting emit very high levels of Blue-Violet light (415 – 455 nm). Even sunlight emits high levels of harmful Blue-Violet light.

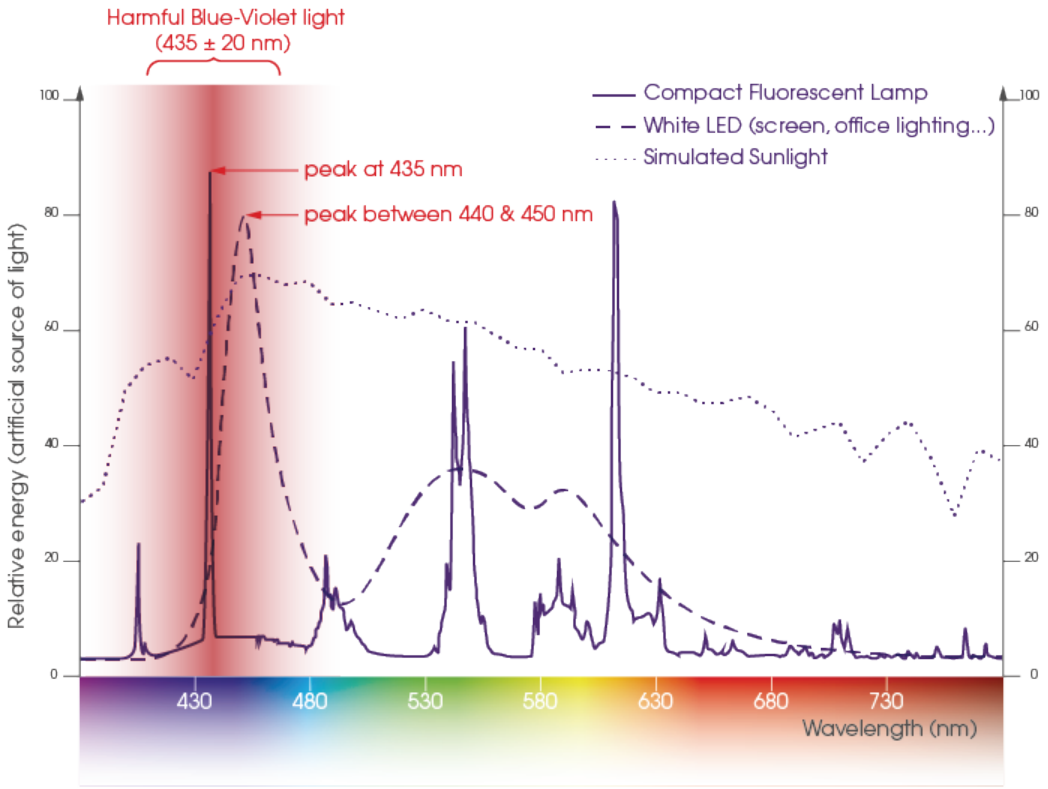

Figure: Emission of visible light at different wavelengths

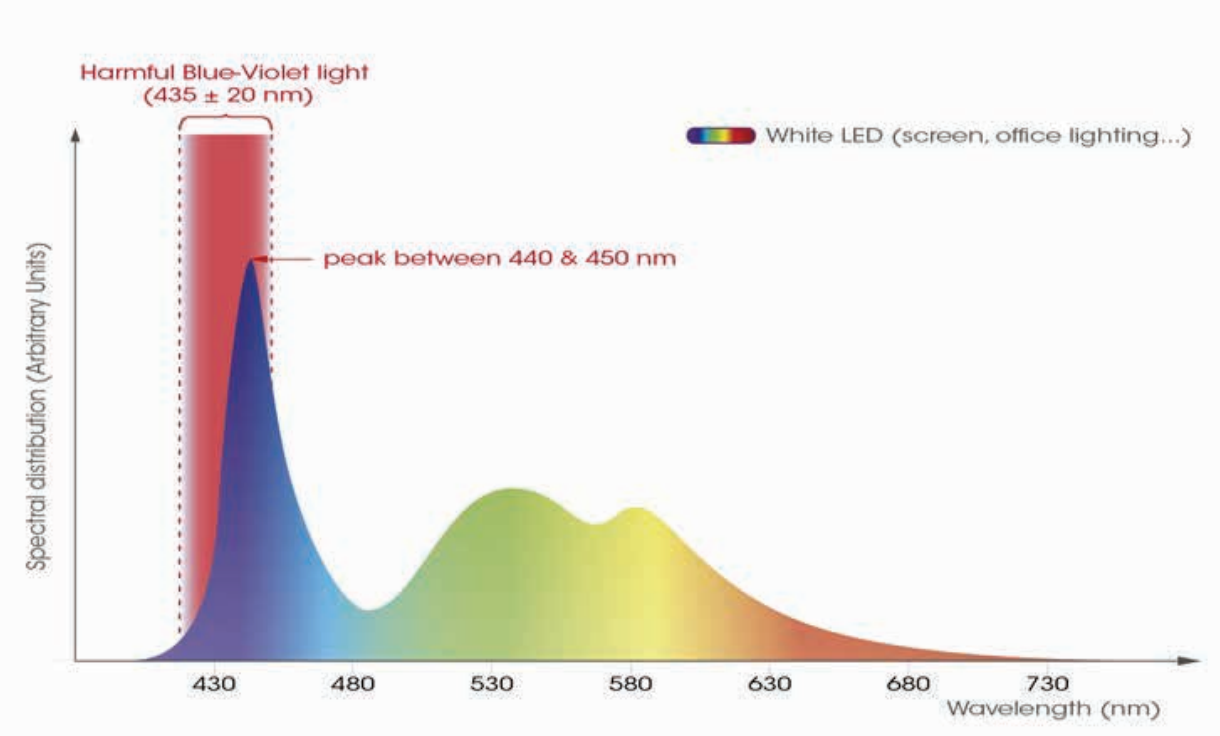

Figure: Emission of visible light at different wavelengths

11. What is the percentage of Blue-Violet light exposure indoor and outdoor?

It is really tricky to determine precisely the distribution of outdoor vs. indoor exposure to Blue-Violet light, because it depends on many environmental and behavioral factors: season, time of day, geographic location, eye movements, distance of use, light source characteristics, reflectance properties of the room surfaces, activities etc.

Nevertheless, some simplified light exposure models can be constructed, based on typical profiles.

We know that the blue light in daylight varies between 25% and 30%. As the sun is the most powerful light source, and whatever the weather (clear or cloudy), protection against its harmful rays, is necessary, even with clear lenses,.

New artificial light sources present a great proportion of blue light in the visible spectrum. Typically, compact fluorescent lamps contain 26% of blue light, cool white LEDs at least 35% versus only 3% for incandescent lamps. Thus, wearing protective lenses against harmful Blue-Violet light is recommended.

III. Product

1. What is Crizal® Prevencia™?

Crizal Prevencia is a No-Glare lens treatment that has exclusive Light Scan™, a **selective** No-Glare technology that works 3 ways:

- Selectively filters out harmful light – Both Blue-Violet and UV light
- Allows beneficial light to pass through – Visible light including Blue-Turquoise light
- Maintains excellent transparency – Clear No-Glare lens for optimal vision at all times

2. What is the front-side reflection/transmission?

Crizal Prevencia lenses have a reformulated AR stack on the front-side of the lens:

- Selectively defect 20% of the harmful Blue-Violet light
- Block UV light (Assuming Crizal Prevencia on a polycarbonate/high-index lens material, or any Transitions® lens)
- Allow beneficial visible light to pass through
- Maintain excellent transparency

Crizal Prevencia lenses offer the same visual transmission of 99% (light for sight) like the other Crizal® products. The visual reflection (Rv) is also lowest at 0.6%.

3. How does a Blue-Violet reflective lens like Crizal Prevencia keep the same low visual reflection (0.6%) as the existing products in the Crizal® portfolio?

The eye is more sensitive to colors in the middle of the spectrum (green, yellow), than those close to the edges of its perception limits (eyes cannot perceive at all ultraviolet and infrared).

The standard measurement of AR efficiency is called Rv, or visual reflection. This measurement combines the reflection of the AR along the visible spectrum, from 380 nm (violet) to 780 nm (red), with the sensitivity of the eyes to these different wavelengths. Obviously, the eye is more sensitive to colors in the middle of the spectrum (green), than close to the edges of its perception limits (eyes cannot perceive at all ultraviolet and infrared).

Crizal® Prevencia™ lenses show intentionally a higher reflection in Blue-Violet spectrum, which is the harmful for the retina. It has a low impact on Rv since these rays are less perceived by the photoreceptors than green & yellow light. Crizal® Prevencia™ is less reflective than other Crizal® products across the rest of the spectrum leading ultimately to an equivalent visual reflection (Rv=0.6%)

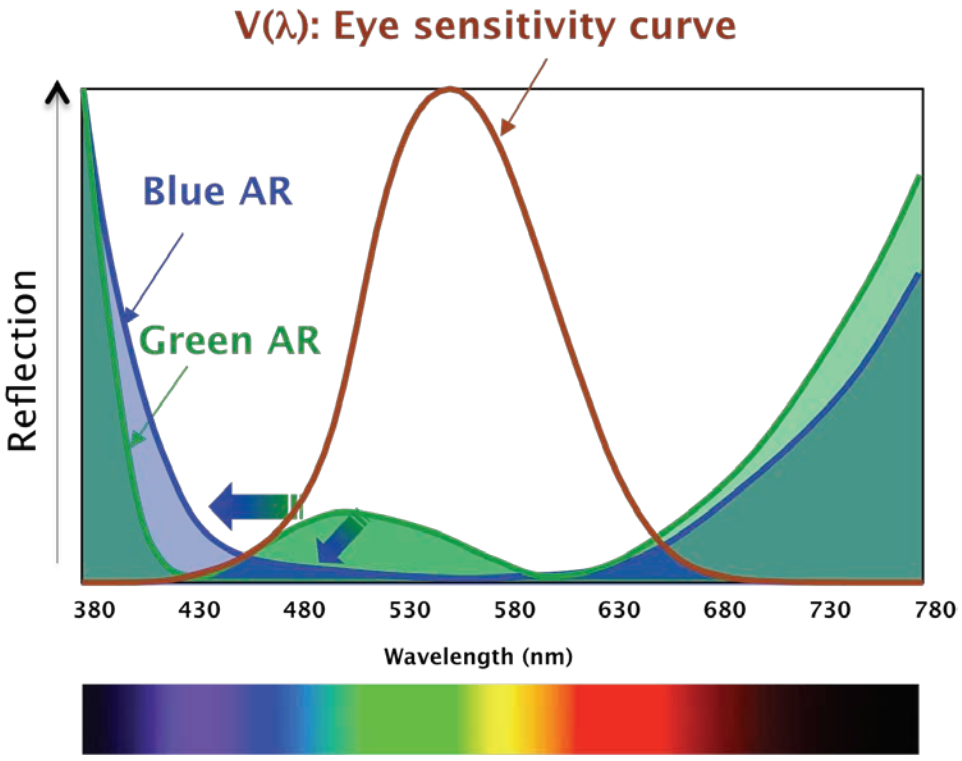

Image for Illustration purposes only

4. How is the performance of Crizal Prevencia with a Transitions® lens?

Crizal Prevencia is compatible with Transitions lenses. When activated outdoors (i.e. in the dark state), a Transitions lens with Crizal Prevencia allows approximately 3% more visible light transmission through the lens than other Transitions lenses. This technical difference will result in the lens getting not quite as dark when activated. However, this difference in transmission is minimal and not perceivable to the eye. Other than the very slight 3% difference, the overall performance of a Transitions lens with Crizal Prevencia is no different from any other Transitions lenses with a Crizal treatment applied.

5. What is the backside reflection protection?

Crizal Prevencia lenses have the same stack on the backside as Crizal Avancé UV™.

Crizal Prevencia lenses feature an Eye Sun Protection (E-SPF®) factor of 25, thus protecting the wearers' eyes with 25X more protection that with no lens at all.[13]

The backside UV light reflection is virtually eliminated (~4%). The backside Blue-Violet light reflection is also minimal (just like UV).

6. Is it really impactful to deflect 20% of the harmful Blue-Violet light on the front-side of the lens?

During *in vitro* experiments conducted by Essilor and Paris Vision Institute, porcine (swine) retinal cells* were exposed to Blue-Violet light, reproducing the physiological exposure to sunlight of the human eye of a 40 year old.

Recent lab tests showed that with Crizal® Prevencia™ deflecting 20[14]% of the Blue-Violet light, retinal cell* death **declined by 25[15]%.**

The deflection of Blue-Violet light by 20% is a deflection of the cumulative exposure to the harmful Blue-Violet light. Considering the cumulative protection provided by Crizal Prevencia lenses, 20% reduction in exposure to Blue-Violet light is significant.

*RPE (Retinal Pigment Epithelium)

[13] E-SPF is a global index developed by Essilor, endorsed by independent third parties, measuring the lens' UV protection excluding direct eye exposure from around the lens. E-SPF of 25 means the wearer is 25 times more protected than without any lens. E-SPF of 25 when Crizal is made with any lens aterial other than clear 1.5 plastic.

[14] Cut of 20% for all Crizal Prevencia lenses except Essilor Orma and Essilor Airwear (% of Blue-violet light cut for these lenses to be confirmed)

[15] Retinal cell death rate declined by 25%, with a cut of 20% for all Crizal Prevencia lenses except Essilor Orma and Essilor Airwear (% of Blue-violet light cut for these lenses to be confirmed). Based on tests conducted on swine (pig) retinal cells.

7. Why is reflection of Blue-Violet light on the backside not a threat to the eye?

Crizal Prevencia No-Glare lens treatment is optimized to limit Blue-Violet reflection on the backside of the lens, at angles around 45°, to only ~4%.

Blue-Violet light is known to damage the backside of the eye namely the retina. The angle of incidence of the Blue-Violet light on the backside prevents the light to reach the retina, thus posing very little to no threat to the eye/retina.

UV light on the other hand, damages the front-side of the eye. Hence, UV reflection is a much bigger threat on the backside of the lens since the reflected UV light falls directly on the front-side of the eye.

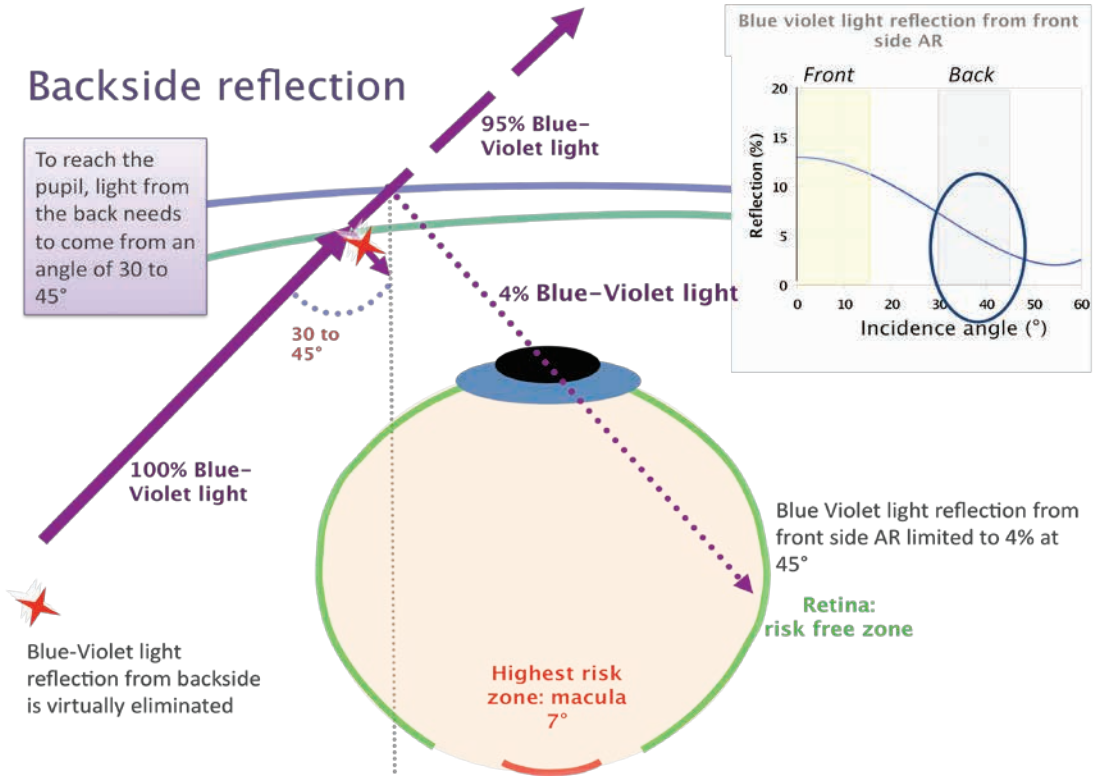

Image for Illustration purposes only

8. How is Crizal Prevencia different from the current "blue-blockers"?

Crizal Prevencia lenses **selectively** deflect harmful Blue-Violet light while allowing the beneficial light (Blue-Turquoise) to pass through. Other "blue-blockers" indiscriminately block all blue light (good and bad). Thus they block the part of visible light that is beneficial for our everyday health and vision. Due to blocking of all blue light, "blue-blockers" may also cause distortion in color perception.