ANSES Opinion
Request No 2019-SA-0139

The Director General

Maisons-Alfort, 17 July 2020

OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

on "blue-light exposure limits for the general population"

ANSES undertakes independent and pluralistic scientific expert assessments.

ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.

It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are published on its website. This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 17 July 2020 shall prevail.

On 30 July 2019, ANSES received a request from the Directorate General for Health to provide scientific arguments supporting a request to the European Commission to revise the exposure limits (ELs) for visible light[1].

1. BACKGROUND AND PURPOSE OF THE REQUEST

On 12 July 2018, the European Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) published a report[2] on the potential risks to human health associated with light-emitting diodes (LEDs).

[1] Incoherent optical radiation from natural and artificial sources, with the exception of lasers.

[2] "*Opinion on potential risks to human health of Light Emitting Diodes (LEDs)*" https://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scheer_consultation_05_en.

Concerning the toxic effects of the light emitted by LED systems, SCHEER:

- underlined that studies in animals (*in vivo* and *in vitro*) have found phototoxic effects associated with exposure to these systems, which raises concerns, especially in terms of effects on eyesight for sensitive population groups (children, adolescents and the elderly);
- nonetheless specified that the exposure conditions in these studies were unrealistic, as the exposure levels exceeded those likely to be reached with domestic LED lighting systems.

Thus, SCHEER concluded that in terms of phototoxicity, there was no evidence of direct adverse health effects due to exposure to LEDs when used in normal conditions by the general population; it also added that domestic LED lighting complies with the current regulations (restrictions on marketing according to the photobiological risk group, determined based on the retinal exposure limits established by the International Commission on Non-Ionizing Radiation Protection (ICNIRP)).

However, the photobiological risk associated with exposure to LEDs was assessed by SCHEER based on the exposure limits for light updated by ICNIRP in 2013; it had not called into question their relevance with regard to the new scientific data available.

On 14 May 2019, having received a formal request to update its previous opinion on the health effects of LEDs, ANSES published an opinion on the "effects on human health and the environment (fauna and flora) of systems using light-emitting diodes (LEDs)"[3]. ANSES noted, in the same spirit as SCHEER, that domestic LED lighting should comply with the regulations in force restricting the public's access to lamps to those in risk group 0 or 1. The Agency also broadened the scope of its expert appraisal on LED lighting to include blue light, focusing on human exposure to this blue light and its phototoxic effects, as well as its effects related to short- and long-term circadian rhythm disruption.

Regarding the phototoxic effects of blue light, ANSES concluded that:

- the retinal phototoxicity of acute exposure to blue-rich light is proven. The contribution of chronic (for several years) retinal exposure to blue-rich light to the occurrence of age-related macular degeneration (ARMD) is also proven;
- it is necessary to revise the exposure limits for optical radiation proposed by ICNIRP, so as to make them sufficiently protective against phototoxic risks (for the general population and for workers).

Indeed, new studies identified by the review of knowledge had raised doubts as to the validity of the exposure limits selected by ICNIRP for the retinal toxicity of light. Some authors (Hunter *et al.*, 2012) considered that to be protective, these exposure limits would need to decrease by a factor of 20. In addition, the expert appraisal highlighted that these ELs are only proposed for acute exposure (for less than eight hours) and ignore the issue of the effects of long-term exposure.

Thus, in light of the apparent discrepancy between the SCHEER and ANSES opinions concerning the assessment of phototoxic risks associated with exposure to blue light, the Directorate General for Health submitted a formal request to ANSES to provide scientific arguments supporting a request to the European Commission to revise the exposure limits.

2. ORGANISATION AND METHODOLOGY OF THE EXPERT APPRAISAL

This expert appraisal falls within the sphere of competence of the Expert Committee (CES) on "Physical agents, new technologies and development areas". It was carried out in accordance with French standard NF X 50-110 "Quality in Expert Appraisals – General Requirements of Competence for Expert Appraisals (May 2003)".

[3] https://www.anses.fr/en/content/leds-blue-light.

The expert appraisal was undertaken with the scientific support of three expert rapporteurs specialising in optical radiation and its effects on vision. The methodology and expert appraisal work were presented to the CES at meetings on 23 January 2020 and 3 March 2020.

Interests declared by the experts were analysed by ANSES before they were appointed and throughout their work in order to prevent risks of conflicts of interest in relation to the points addressed in the expert appraisal. The experts' declarations of interests have been made public via the following website: https://dpi.sante.gouv.fr.

3. ANALYSIS AND CONCLUSIONS OF THE CES

3.1. Establishment of exposure limits for light

ICNIRP is an international scientific commission whose aim is to protect people and the environment against the adverse effects of non-ionising radiation. Among other things, ICNIRP has published guidelines proposing exposure limits for incoherent optical radiation[4], with the goal of preventing adverse photobiological effects on the eyes and skin.

In the area of lighting, in particular that of light produced by LEDs, the ICNIRP recommendations to be taken into account are the ICNIRP Guidelines on Limits of Exposure to Incoherent Visible and Infrared Radiation, published in 2005 and updated in 2013.

To establish its guidelines aiming to protect health, ICNIRP mentions two possible types of retinal damage:

- Type I: damage to the retina (burn) resulting from prolonged exposure to very bright light (Noell *et al.,* 1966; Williams and Howell, 1983; Mellerio *et al.*, 1994). This effect is linked to damage to the photoreceptors as a result of prolonged photobleaching of rhodopsin.
- Type II: photochemical damage to the retina caused specifically by blue light. This effect is related to blue-light absorption by the retinal pigment epithelium (RPE) (Ham *et al*., 1976; Ham *et al*.,1989; Lund *et al*., 2006). This type of damage is referred to as blue-light hazard (Sliney and Wolbarsht, 1980).

When studying the effects of blue light on the retina, only type II photochemical retinal damage should be considered. This is involved in particular in vision loss, age-related macular degeneration (ARMD), etc.

- *Photochemical damage related to blue light*

ICNIRP distinguishes between two population groups when it comes to sensitivity to blue light:

- aphakic (without lens) or pseudophakic (with artificial lenses) individuals and children under the age of two, for whom sensitivity extends to 300 nm in the ultraviolet range;
- the general population, i.e. people over the age of two having a healthy lens, for whom photochemical damage to the retina due to exposure to blue light is induced by radiation mainly in the 380 nm (blue-ultraviolet limit) to 550 nm range.

Curves A(λ) and B(λ) below represent sensitivity to blue light for these two population groups, according to wavelength.

[4] Only lasers emit coherent light (phase coherence); all other light sources are incoherent sources.

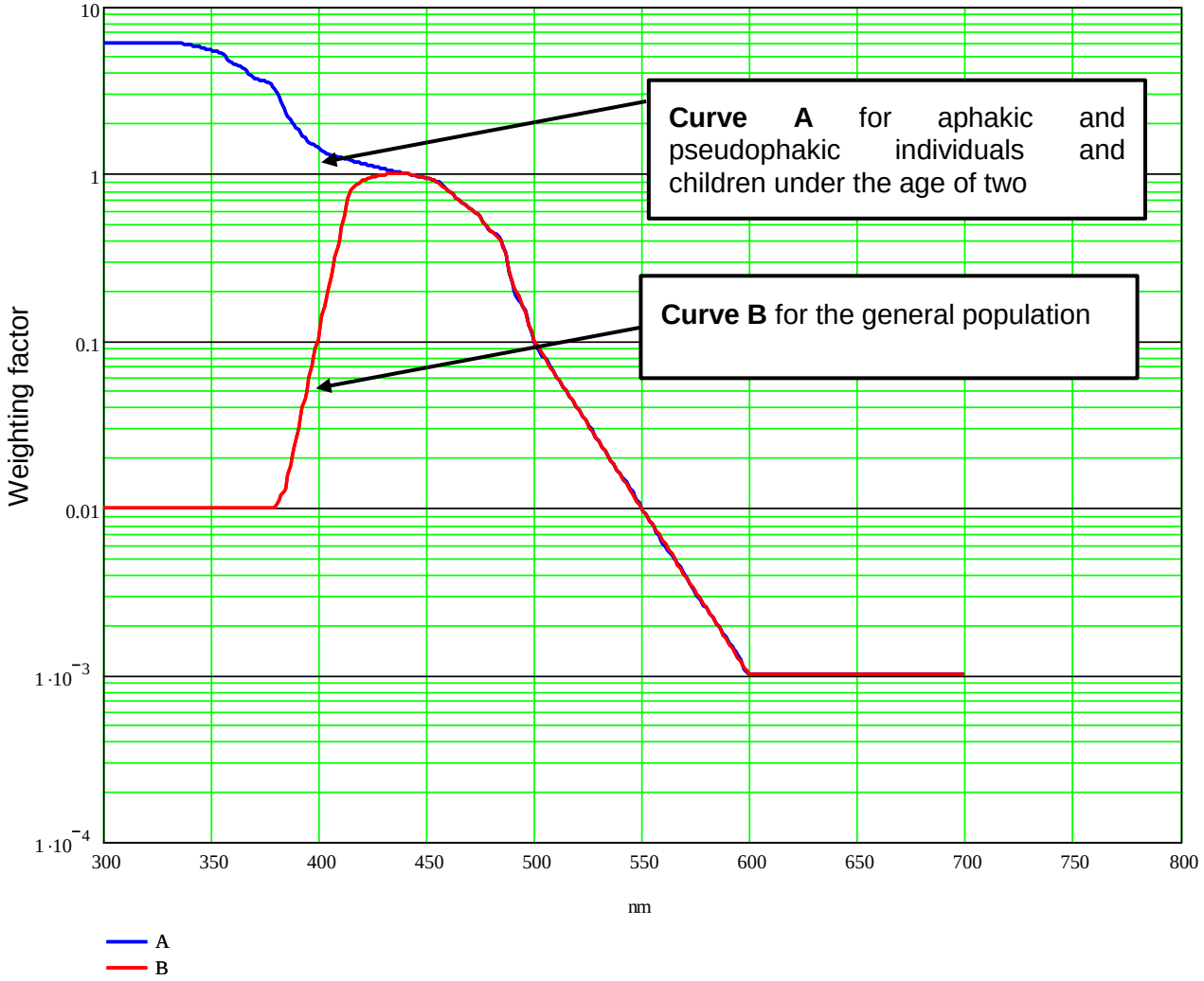

Figure 1: Spectral weighting curves for retinal sensitivity to blue light

- *Establishment of blue-light exposure limits*

The studies by Ham (Ham *et al*., 1976; Ham *et al*., 1989) enabled ICNIRP to establish acute exposure thresholds for blue light from which retinal lesions have been observed in macaques. These thresholds are around 20 to 30 J/cm². ICNIRP converted these thresholds into human exposure limits using a simple geometric model of the human eye (Gullstrand's model), considering a focal length of 17 mm, transmittance in the ocular media in front of the retina of 0.9 and a pupil diameter of 3 mm (pupil considered as constricted in bright light). A safety factor of 5 to 10 was applied to these retinal exposure limits.

Depending on the duration of exposure, the exposure limits are expressed differently:

- for exposure durations of less than 10,000 seconds (2.8 hours), ICNIRP proposes a blue-light weighted energy dose received by the retina as an indicator. The EL is as follows:

$H_r = 2.2$ J/cm² (where H_r is radiant exposure)

- for longer durations of exposure, of more than 10,000 seconds, exposure is no longer expressed as a dose but as blue-light weighted retinal irradiance. The EL is then as follows:

E_r = 0.22 mW/cm² (where E_r is irradiance)

ICNIRP recommends using curve A(λ) for children under the age of two and for aphakic individuals in particular, and curve B(λ) to assess retinal exposure to blue light from the age of two.

Several aspects of the ICNIRP guidelines currently raise questions:

- the age limit of two years, below which, to assess retinal exposure, it is recommended to use curve A(λ), which is more protective than curve B(λ). In reality, there are no physiological arguments enabling two years to be set as the age from which the lens effectively filters the shortest wavelengths. This age merely corresponds to the end of eyeball growth and does not refer to the lens's blue-light filtration capacity (Charman *et al.*, 2003; Weale *et al*., 1988; Sample *et al.*, 1991);
- the blue-light exposure limits were established based on experiments conducted with the means of observation and measurement available in the 1980s (with low sensitivity);
- the INCIRP recommendations do not seem to take into account the possible aggravation of the consequences of retinal exposure to blue light when the pupil is abnormally dilated, for example in situations of low light (reduced pupillary reflex). This can occur in the event of general lighting with short wavelengths (especially in the blue-light range) producing low visual stimulation and low excitation of melanopsin-expressing ganglion cells;
- the choice of the 10,000-second value from which the EL is expressed as irradiance is not explained.

3.2 Arguments in favour of updating the blue-light exposure limits

Below, ANSES sets out various arguments justifying the revision of the ELs for blue light:

(1) Since the publication of the studies by Ham (Ham *et al.*; 1976 and 1989), new techniques for detecting phototoxicity have become much more sensitive. These techniques now enable the earlier detection of retinal cells destroyed by apoptosis following exposure to blue light.
(2) Subject to certain precautions, it seems useful to consider new findings from experiments in rodents, which suggest overestimation of the retinal doses likely to induce acute toxicity.
(3) The cumulative effects of repeated long-term exposure should be considered. This point is of prime importance when considering type II photochemical effects, which generate oxidative stress whose effects are cumulative.
(4) It is important to take into account the biological rhythms of the retina, which is more sensitive to light (natural and artificial) at night.
(5) The most recent research underlines the possible positive effects of exposure to red light. Therefore, when assessing the phototoxicity of lighting, it is necessary to take into consideration not only the presence of blue radiation in the spectrum but also the amount of photoprotective red light. In other words, the spectral composition of light should be considered.

These various points are explained in detail below.

Increased sensitivity of recent techniques for detecting phototoxicity

The doses of energy from which retinal lesions are observed vary depending on the wavelength, the studied species, the experimental conditions, and the biological indicator used to define toxicity.

Four main methods of detecting phototoxicity have been used in animal studies. These methods are described below. The first two – direct retinal examination and full-field electroretinography (ERG) – are old and non-invasive and have low sensitivity. The latter two – histological sections and techniques for detecting cell death – are more recent and more sensitive.

- *Direct retinal examination*

During a direct retinal examination, a beam of light is projected onto the surface of the retina which is then macroscopically observed.

- *Full-field electroretinography*

Full-field electroretinography is an electrophysiology technique that records electrical potentials generated by the retina in response to a light stimulus. It is widely used in humans and even more so in animals to assess retinal integrity. The usefulness of this technique is undeniable but it has low sensitivity. ERG signals are reduced when retinal damage is very severe (Machida *et al.,* 2000).

- *Histological section*

Retinal analysis from coloured histological sections enables tissue condition to be evaluated. This method is widely used to assess the thickness of the outer nuclear layer, which contains the photoreceptor nuclei and thins in the event of light-induced degeneration. However, this thinning can be delayed, occurring several months following acute exposure (Garcia-Ayuso *et al.,* 2011), masking toxic effects when the analysis is undertaken too early.

- *Techniques for detecting cell death*

These methods enable toxic cellular effects to be identified. One widely used technique is the terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL) method, which identifies apoptotic DNA fragmentation. An enzymatic step is necessary to identify cell death caused by various types of apoptosis (Lebon *et al.,* 2015). Other markers can be used to quantify cell death resulting from other mechanisms (necrosis, autophagy, etc.).

Most of the studies used to define blue-light exposure limits are based on exploration methods with low sensitivity and/or on ERG; these methods are unable to detect cellular lesions that can have real functional consequences.

Consideration of new findings from experiments on rodents

To establish exposure limits for blue light, findings from studies on macaques have been used to get as close as possible to the human retina. However, for ethical reasons[5], the use of non-human primates is currently limited. New data have been obtained with rodents, using more sensitive methods for assessing phototoxicity. These data cannot be discarded on the grounds that the retina of rodents is different from that of primates and humans.

There is a difference in retinal sensitivity between primates and rodents; it has been explained, at least partially, by the difference in chromatin structure in the rod nuclei of the various species. In rodents, which are generally nocturnal, chromatin is highly condensed in the centre of the nucleus, which limits photon diffraction and thus optimises vision in darkness (Solovei *et al*., 2009). Conversely, in human and non-human primates, chromatin in rods is dispersed, limiting photon penetration. Moreover, rodents have higher sensitivity in the UV range (unlike humans, for whom this radiation is not visible); lastly, rodents do not have a macula.

Since the studies by Ham *et al.* (1976, 1989) and in the absence of new data in macaques, it has seemed relevant to use the available data in rodents, based on the concept of retinal dose as

[5] In order for the experimental use of live animals to be authorised, European and French law requires that a number of conditions be met. Thanks to harmonisation efforts at European level, European Convention STE 123 and Decree No. 2001-486 as well as Directive 2010/63/EU and Decree No. 2013-118 express the same requirements, even though they are not always formulated in the same way.

proposed by van Norren and Gorgels (van Norren and Gorgels, 2011). Indeed, studies aiming to assess the phototoxicity of light are carried out in widely varying experimental conditions (animal species, exposure time, luminance, wavelength, etc.), making it difficult to compare the results. The retinal dose helps eliminate these differences so that various experiments can be compared. Van Norren and Gorgels collected data from numerous studies undertaken in different species and homogenised them to deduce the retinal dose. They showed that the retina of rodents is twice as sensitive to light than that of primates. However, no controlled comparative prospective studies were undertaken to define an exact factor.

Need to take into account the cumulative effects of long-term exposure

The current blue-light exposure limits do not take into account the possible effects of accumulated infraclinical lesions (with no clinically visible symptoms) associated with chronic exposure. This type of lesion may induce accelerated ageing or be toxic to the retina. In the event of type II phototoxicity, oxidative stress causes stable modifications in cell components that are not clinically detectable; however, the accumulation of these changes induces delayed lesions. Moreover, with age, the accumulation of lipofuscin[6] and melanolipofuscin (combination of melanin and lipofuscin) in RPE cells increases the risk of oxidative stress, as they are photosensitising (Wing *et al.,* 1978).

Epidemiological data support this position. They have shown that prolonged exposure to sunlight, especially at a young age, leads to an increased risk of ARMD; this is particularly true for the blue component, which is toxic to the retina[1] (see ANSES LED report, 2019). Thus, the accumulation of oxidative stress over several years, during the day (with sunlight and/or artificial light) and in the evening or at night (exposure to artificial light at a time when, physiologically, the retina has adjusted to night vision), is associated with an increased risk of lesions.

Acute and chronic lesions can differ in nature, as has been demonstrated on the skin after decades of research on the topic.

Need to take retinal rhythms into account

The circadian system of humans includes a main clock and peripheral clocks in various organs. The retina has its own circadian clock. It therefore works in different ways over the course of a day, to adjust to different day and night light environments. In the middle of the night, for example, the retina is more sensitive so it can detect the slightest photon and use this information to respond.

The retina adjusts its sensitivity through molecular and cellular modifications regulated by the endogenous clock. For example, during the night, rods and cones are interconnected via gap junctions, causing the system to be more sensitive. Conversely, during the day, photoreceptors are isolated from one another (Ribelayga *et al.*, 2008). Similarly, the affinity of ion channels increases at night and visual sensitivity is higher (Bassi & Powers, 1987; Ko *et al.*, 2001).

A large number of processes essential for visual physiology are thus regulated by an endogenous retinal clock: molecular and cellular modifications, synthesis of visual pigments, melatonin and dopamine synthesis, photoreceptor phagocytosis and melanopsin synthesis (McMahon *et al.*, 2014). Special attention should be paid to taking these phenomena into account when establishing exposure limits.

[6] Lipofuscin is a brown cellular pigment made up of molecular waste. It is found in senescent or degenerating epithelial and connective cells.

Synergies between various wavelengths

In its opinion of April 2019 on the "effects on human health and the environment (fauna and flora) of systems using light-emitting diodes (LEDs)", ANSES particularly stressed the fact that red light can have photoprotective effects in humans.

Ham *et al.* (Ham *et al*., 1989; Ham *et al*., 1976) showed that blue light mainly affects the pigments contained in the cells of the retinal pigment epithelium. However, the authors considered the bands of the spectrum separately, which is not relevant when assessing polychromatic light. Various wavelengths will have specific effects depending on the cell and the cellular component of the retina, but synergies between all these wavelengths will determine whether or not they have adverse effects on the retina. For example, wavelengths in the red part of the visible spectrum, above 600 nm, modify the mitochondrial activity of cells and reduce the effects of oxidative stress (Merry *et al.,* 2017) induced by other wavelengths.

Thus, the harmful effects of blue light can be modulated by the amount of red light contained in the spectrum in question. This suggests it is important, when analysing the phototoxicity of a light, to properly take into account the various wavelengths present (blue, red, etc.). It should be noted that the current emission spectra of the LEDs used in lighting contain very little red light compared to the spectra of daylight and incandescent lamps. The spectral imbalance in favour of blue light may cause it to induce oxidative stress.

3.3 Better consideration of young populations

The sensitivity of the eye, which varies with age, should be better taken into consideration. It is necessary to better protect children, adolescents and young adults (accounting for around 25% of the French population[7]), who are more vulnerable to the hazards of blue light because their lens is not as effective at filtering it.

The human eye is capable of perceiving optical radiation with wavelengths of 400 to 700 nm. The cornea absorbs most radiation below 295 nm, which includes UVC radiation, more than 90% of UVB radiation and 35% to 40% of UVA radiation. The lens absorbs UVA and UVB radiation that has crossed the cornea, as well as short wavelengths and infrared radiation. Physiologically, the lens acts as a natural filter by absorbing radiation with wavelengths below 400 nm.

However, the lens's filtration capacity depends on age (Kessel *et al,* 2010; Turner and Mainster, 2008). Before the age of eight, only 20% of wavelengths from 380 to 500 nm are filtered. This filtration capacity increases with age: at the age of 25, 80% of wavelengths below 400 nm and 50% of wavelengths from 400 to 500 nm are filtered.

Due to the lens's lower filtration capacity, the amount of blue light received by a child's retina, and therefore the level of exposure, is higher than that received by an adult's retina. This point must be taken into account when assessing the risks associated with blue light.

Currently, ICNIRP only issues a specific recommendation for children under the age of two aiming to encourage use of curve A when assessing risks. However, this age seems arbitrary from a physiological standpoint and causes risks to be underestimated for children over the age of two through to adulthood.

[7] Source: INSEE, 2019.

3.4 Conclusions

Considering that:

- the parameters chosen to establish retinal exposure limits are based on low-sensitivity methods unable to detect lesions that can have real (immediate and long-term) functional consequences;
- there are new studies in animals, especially rodents, suggesting that acute toxicity can be induced at exposure levels below the current limits;
- chronic exposure to light needs to be taken into account;
- retinal rhythms need to be considered, with increased sensitivity during exposure at night;
- synergies between wavelengths of light need to be taken into account;

the CES is repeating its recommendation to reassess the exposure limits proposed by ICNIRP for the risks associated with exposure to blue light.

Moreover, the CES recommends taking into account, in this reassessment, specific risks in young populations, due in particular to the lower capacity of their lens to filter blue light.

To that end, the CES recommends conducting further studies and research on the phototoxicity of light, ensuring the implementation of appropriate, reproducible experimental measurement protocols that can be extrapolated to humans. These protocols should call on new technologies for detecting phototoxicity and consider the full emission spectrum of the light source as well as chronic exposure (during the day and at night).

Until new experimental scientific results become available for redefining blue-light exposure limits, and to better consider sensitive population groups, the CES recommends using the more protective weighting curve A for the entire population when defining risk groups according to the NF 62471 photobiological safety standard.

More broadly, lifelong exposure to all environmental factors should be taken into account when assessing health risks. Regarding exposure to light, its interactions with photosensitising compounds, such as dyes and certain medications, should also be considered.

4. AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety endorses the conclusions and recommendations of the CES on “Physical agents, new technologies and development areas”.

Dr Roger Genet

KEYWORDS

Lumière bleue, LED, éclairage artificiel, phototoxicité, enfants, valeurs limites, exposition

Blue light, LED, artificial lighting, phototoxicity, children, exposure limits, exposure

REFERENCES

ANSES. 2019. “Effects on human health and the environment (fauna and flora) of systems using light-emitting diodes (LEDs), ANSES Opinion, Collective expert appraisal reports, Scientific edition”, 2019.

Bassi, C. J., and M. K. Powers. 1987. “Circadian Rhythm in Goldfish Visual Sensitivity”. Investigative Ophthalmology & Visual Science 28 (11): 1811-15.

Charman, W.N. 2003. “Age, lens transmittance, and the possible effects of light on melatonin suppression”. Ophthalmic and Physiological Optics 23 (2): 181-87. https://doi.org/10.1046/j.1475-1313.2003.00105.x.

García-Ayuso, D., M. Salinas-Navarro, M. Agudo-Barriuso, L. Alarcón-Martínez, M. Vidal-Sanz, and M.P. Villegas-Pérez. 2011. “Retinal ganglion cell axonal compression by retinal vessels in light induced retinal degeneration”. Molecular Vision 17: 1716-33.

Ham, W. T. 1989. “The photopathology and nature of the blue-light and near-UV retinal lesion produced by lasers and other optical sources, In: Laser Applications in Medicine and Biology, edited by M.L. Wolbarsht, New-York Publishing Corp.”, 1989.

Ham, William T., Harold A. Mueller, and David H. Sliney. 1976. “Retinal Sensitivity to Damage from Short Wavelength Light”. Nature 260 (5547): 153-55. https://doi.org/10.1038/260153a0.

Hunter, Jennifer J, Jessica I W Morgan, William H Merigan, David H Sliney, Janet R Sparrow, and David R Williams. 2012. “The susceptibility of the retina to photochemical damage from visible light”. Progress in Retinal and Eye Research 31 (1): 28-42. https://doi.org/10.1016/j.preteyeres.2011.11.001.

ICNIRP David Sliney, Danielle Aron-Rosa, Francois DeLori, Franz Fankhauser, Robert Landry, Martin Mainster, John Marshall, et al. 2005. “Adjustment of Guidelines for Exposure of the Eye to Optical Radiation from Ocular Instruments: Statement from a Task Group of the International Commission on Non-Ionizing Radiation Protection (ICNIRP)”. *Applied Optics* 44 (11): 2162-76. https://doi.org/10.1364/AO.44.002162.

ICNIRP, International Commission on Non-Ionizing Radiation. 2013. “ICNIRP Guidelines on Limits of Exposure to Incoherent Visible and Infrared Radiation”. Health Physics 105 (1): 74. https://doi.org/10.1097/HP.0b013e318289a611.

Kessel, Line, Jesper Holm Lundeman, Kristina Herbst, Thomas Vestergaard Andersen, and Michael Larsen. 2010. “Age-Related Changes in the Transmission Properties of the Human Lens and Their Relevance to Circadian Entrainment”. Journal of Cataract & Refractive Surgery 36 (2): 308-12. https://doi.org/10.1016/j.jcrs.2009.08.035.

Ko, G. Y., M. L. Ko, and S. E. Dryer. 2001. “Circadian Regulation of CGMP-Gated Cationic Channels of Chick Retinal Cones. Erk MAP Kinase and Ca2+/Calmodulin-Dependent Protein Kinase II”. Neuron 29 (1): 255-66.

Lebon, Cecile, Gloria Villalpando Rodriguez, Ikram El Zaoui, Imene Jaadane, Francine Behar-Cohen, and Alicia Torriglia. 2015. “On the Use of an Appropriate TdT-Mediated DUTP-Biotin Nick End Labeling Assay to Identify Apoptotic Cells”. Analytical Biochemistry 480 (July): 37-41. https://doi.org/10.1016/j.ab.2015.04.007.

Lund, David J., Bruce E. Stuck, and Peter Edsall. 2006. “Retinal Injury Thresholds for Blue Wavelength Lasers”. Health Physics 90 (5): 477-84. https://doi.org/10.1097/01.HP.0000190115.83416.cb.

Machida, S., M. Kondo, J.A. Jamison, N.W. Khan, L.T. Kononen, T. Sugawara, R.A. Bush, and P.A. Sieving. 2000. “P23H rhodopsin transgenic rat: Correlation of retinal function with histopathology”. Investigative Ophthalmology and Visual Science 41 (10): 3200-3209.

McMahon, Douglas G., P. Michael Iuvone, and Gianluca Tosini. 2014. “Circadian Organization of the Mammalian Retina: From Gene Regulation to Physiology and Diseases”. Progress in Retinal and Eye Research 39 (March): 58-76. https://doi.org/10.1016/j.preteyeres.2013.12.001.

Mellerio. 1994. “Light effects on the retina. In Principles and Practice of Ophthalmology: Basic Science. D. M. Albert and F. A. Jakobiec, editors. W.B. Saunders Co, Philadelphia. 1326–1345”, 1994.

Merry, G.F., M.R. Munk, R.S. Dotson, M.G. Walker, and R.G. Devenyi. 2017. “Photobiomodulation reduces drusen volume and improves visual acuity and contrast sensitivity in dry age-related macular degeneration”. Acta Ophthalmologica 95 (4): e270-77. https://doi.org/10.1111/aos.13354.

Morgan, Jessica I. W., Jennifer J. Hunter, Benjamin Masella, Robert Wolfe, Daniel C. Gray, William H. Merigan, François C. Delori, and David R. Williams. 2008. “Light-Induced Retinal Changes Observed with High-Resolution Autofluorescence Imaging of the Retinal Pigment Epithelium”. Investigative Ophthalmology & Visual Science 49 (8): 3715-29. https://doi.org/10.1167/iovs.07-1430.

Noell, Werner K., Virgil S. Walker, Bok Soon Kang, and Steven Berman. 1966. “Retinal Damage by Light in Rats”. Investigative Ophthalmology & Visual Science 5 (5): 450-73.

Norren, Dirk van, and Theo G. M. F. Gorgels. 2011. “The Action Spectrum of Photochemical Damage to the Retina: A Review of Monochromatic Threshold Data”. Photochemistry and Photobiology 87 (4): 747-53. https://doi.org/10.1111/j.1751-1097.2011.00921.x.

Ribelayga, Christophe, Yu Cao, and Stuart C. Mangel. 2008. “The Circadian Clock in the Retina Controls Rod-Cone Coupling”. Neuron 59 (5): 790-801. https://doi.org/10.1016/j.neuron.2008.07.017.

Sample, P. A., J. S. Quirante, and R. N. Weinreb. 1991. “Age-Related Changes in the Human Lens. Clinical Assessment of Age-Related Changes in the Human Lens”. Acta Ophthalmologica 69 (3): 310-14. https://doi.org/10.1111/j.1755-3768.1991.tb04820.x.

Sliney, D. H., and J. Mellerio. 1980. Safety with Lasers and Other Optical Sources: A Comprehensive Handbook. Edited by Myron Wolbarsht. Springer US. https://www.springer.com/gp/book/9781489935960.

Sliney, David H. 1982. “Optical Radiation Safety”. Lighting Research & Technology 14 (3): 142-50. https://doi.org/10.1177/096032718201400303.

Solovei, Irina, Moritz Kreysing, Christian Lanctôt, Süleyman Kösem, Leo Peichl, Thomas Cremer, Jochen Guck, and Boris Joffe. 2009. “Nuclear Architecture of Rod Photoreceptor Cells Adapts to Vision in Mammalian Evolution”. Cell 137 (2): 356-68. https://doi.org/10.1016/j.cell.2009.01.052.

Turner, P. L., and M. A. Mainster. 2008. “Circadian Photoreception: Ageing and the Eye’s Important Role in Systemic Health”. British Journal of Ophthalmology 92 (11): 1439-44. https://doi.org/10.1136/bjo.2008.141747.

Weale, R. A. 1988. “Age and the Transmittance of the Human Crystalline Lens”. The Journal of Physiology 395 (January): 577-87. https://doi.org/10.1113/jphysiol.1988.sp016935.

Williams, T. P., and W. L. Howell. 1983. “Action Spectrum of Retinal Light-Damage in Albino Rats”. Investigative Ophthalmology & Visual Science 24 (3): 285-87.

Wing, G.L., G.C. Blanchard, and J.J. Weiter. 1978. “The topography and age relationship of lipofuscin concentration in the retinal pigment epithelium”. Investigative Ophthalmology and Visual Science 17 (7): 601-7.

ANNEX 1: PRESENTATION OF PARTICIPANTS

PREAMBLE: The expert members of the Expert Committees and Working Groups or designated rapporteurs are all appointed in a personal capacity, *intuitu personae*, and do not represent their parent organisation.

ANSES PARTICIPATION

Scientific contribution

Dina ATTIA – Scientific Project Manager, Unit for assessment of risks related to physical agents

Marion BOYER – Scientific Project Leader, Unit for assessment of risks related to physical agents

Olivier MERCKEL – Head of the Unit for assessment of risks related to physical agents

Aurélie NIAUDET – Deputy Head of the Unit for assessment of risks related to physical agents

RAPPORTEURS

Francine BEHAR-COHEN – Research Director at INSERM UMR 1138, Pathophysiology of ocular diseases, Professor of Ophthalmology, Paris-Descartes University, Practitioner at Hôtel Dieu Hospital

Olivier ENOUF – Engineer in metrology of optical radiation and optical safety testing of laser products and LEDs – National Metrology and Testing Laboratory (LNE)

Alicia TORRIGLIA – Doctor, Director of Ophthalmology Research, Cordeliers Research Centre, French National Institute for Health and Medical Research (INSERM)

EXPERT COMMITTEE

The work described in this report was monitored and adopted by the Expert Committee (CES) on "Physical agents, new technologies and development areas".

Chair

Anne PEREIRA DE VASCONCELOS – Research Manager, French National Institute for Health and Medical Research (INSERM), Laboratory of Cognitive and Adaptive Neurosciences – UMR 7364, CNRS – University of Strasbourg

Members

Thomas CLAUDEPIERRE – Lecturer and researcher at the University of Lorraine

Brigitte DEBUIRE – Emeritus University Professor

Jean-François DORÉ – Emeritus Research Director at the French National Institute for Health and Medical Research (INSERM)

Thierry DOUKI – Head of Laboratory/Doctor Engineer in Chemistry, French Alternative Energies and Atomic Energy Commission (CEA)

Jack FALCÓN – Emeritus Researcher at the National Centre for Scientific Research (CNRS), specialising in animal chronobiology, Biology of Aquatic Organisms and Ecosystems (BOREA), CNRS 7208, National Museum of Natural History

Emmanuel FLAHAUT – Research Director at the National Centre for Scientific Research (CNRS)

François GAUDAIRE – Engineer at the French Scientific and Technical Centre for Building (CSTB)

Martine HOURS – Physician and Epidemiologist, Research Director at the French Institute of Science and Technology for Transport, Development and Networks (IFSTTAR)

Chaker LARABI – Lecturer and researcher at the University of Poitiers

Joël LELONG – Assistant Laboratory Director / Doctor of Physics, French Institute of Science and Technology for Transport, Development and Networks (IFSTTAR)

Frédérique MOATI – Lecturer in Biophysics and Nuclear Medicine, University Paris Sud XI / Hospital Practitioner / Radiopharmacist / Biologist, AP-HP Bicêtre Hospital

Catherine MOUNEYRAC – Director of the Institute of Biology and Applied Ecology and Professor in Aquatic Ecotoxicology at the Catholic University of the West (UCO)

Fabien NDAGIJIMANA – University Professor, Joseph Fourier University, Grenoble

Anne-Lise PARADIS – Research Manager at the National Centre for Scientific Research (CNRS)

Marie-Pierre ROLS – Research Director at the National Centre for Scientific Research (CNRS)

Valérie SIMONNEAUX – Researcher in Neurobiology of Rhythms at the National Centre for Scientific Research (CNRS)

Alain SOYEZ – Laboratories Manager, Consulting Engineer, Nord-Picardie Occupational Health and Pension Insurance Fund

Esko TOPPILA – Professor, Research Director at the Finnish Institute of Occupational Health

Alicia TORRIGLIA – Doctor, Director of Ophthalmology Research, Cordeliers Research Centre, French National Institute for Health and Medical Research (INSERM)

Françoise VIÉNOT – Professor Emeritus – Centre for Research on Conservation (CRC), National Museum of Natural History, CNRS, Ministry of Culture, 36 rue Geoffroy Saint Hilaire, 75005 Paris, France

Catherine YARDIN – Professor, Head of Department, Doctor and Biologist at Dupuytren Hospital, Limoges University Hospital

ANNEX 2: FORMAL REQUEST LETTER

2019-SA-0139

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

MINISTERE DES SOLIDARITES ET DE LA SANTE

DIRECTION GENERALE DE LA SANTE
Sous-direction Prévention des risques liés à l'environnement et l'alimentation
Bureau EA1 Environnement extérieur et produits chimiques
Tél.01 40 56 50 97 : 154.
Alice.kopel@sante.gouv.fr
D-19-016373

Paris, le 30 JUIL. 2019

COURRIER ARRIVE
02 AOUT 2019
DIRECTION GENERALE

Le Directeur général de la santé

à

Monsieur le Directeur général
de l'Agence nationale de sécurité sanitaire
de l'alimentation, de l'environnement et du travail

Objet : demande d'appui scientifique et technique suite à la publication de l'expertise relative aux effets sur la santé humaine des diodes électroluminescentes (LED)

Faisant suite à une saisine de la DGS, de la DGPR et de la DGCCRF, vous avez publié le 14 mai 2019, la mise à jour de votre expertise de 2010 relative aux effets sur la santé humaine des diodes électroluminescentes (LED).

Le comité d'experts souligne dans ses conclusions, reprises dans votre avis du 5 avril 2019, les effets toxiques d'une lumière riche en bleu sur l'œil. En particulier, il souligne que l'effet phototoxique sur la rétine d'une exposition aiguë (inférieure à 8 heures) à une lumière riche en bleu et l'effet de l'exposition chronique de la rétine (plusieurs années) à une lumière riche en bleu sur la contribution à la survenue de dégénérescence maculaire liée à l'âge (DMLA) sont avérés.

Le comité mentionne que de nombreuses études montrent que les valeurs limites d'exposition (VLE) retenues par l'Icnirp (International Commission on Non-Ionizing Radiation Protection) pour la toxicité rétinienne de la lumière ne sont pas suffisamment protectrices. Certains auteurs (Hunter et al., 2012) ont estimé que ces VLE étaient supérieures d'un facteur 20 par rapport à des valeurs protectrices. De plus, l'expertise a permis de souligner que ces VLE ne sont proposées que pour une exposition aiguë (exposition inférieure à 8 h) et éludent la question d'une exposition à long terme.

En conséquence, vous recommandez dans votre avis de faire évoluer les valeurs limites d'exposition à la lumière bleue, valeurs issues des travaux de l'Icnirp et publiées en 2013 qui ne prennent pas en compte les effets d'une exposition sur le long terme. Ces valeurs sont reprises dans les normes servant à l'évaluation de la sécurité photobiologique des systèmes à LED pour vérifier leur conformité aux exigences essentielles de santé et de sécurité des directives européennes.

14 AVENUE DUQUESNE – 75350 PARIS 07 SP
TÉLÉPHONE : 01 40 56 60 00 – WWW.SOCIAL-SANTE.GOUV.FR

Cependant, le SCHEER (Scientific Committee on Health, Environmental and Emerging Risks), comité scientifique de la Commission européenne, n'allait pas aussi loin dans les conclusions de son rapport publié en 2018 « Potential risks to human health of Light Emitting Diodes (LEDs) ». Le comité scientifique européen concluait *« qu'il n'y a pas de preuve d'effets sanitaires immédiats, pour la population générale, liés à l'exposition aux LEDs dans les conditions normales d'utilisation des lampes »*. Le rapport du SCHEER mentionne les expériences sur les animaux et les études in vitro qui suggèrent qu'une exposition cumulative à la lumière bleue en dessous des niveaux ayant des effets aigus peut également induire des lésions rétiniennes photochimiques. Mais le comité scientifique européen, considérant le manque d'études portant sur la population générale, n'a pas conclu sur les effets possibles relatifs à une exposition cumulée pour la population.

Les autorités françaises souhaitent par conséquent transmettre votre avis à la Commission européenne appelant en particulier son attention sur la nécessaire révision des valeurs limites. A cette fin, je vous demande de me transmettre un argumentaire scientifique qui permettrait d'étayer la demande de révision auprès de la Commission, en particulier au regard de l'écart d'appréciation sur le risque phototoxique entre votre avis et l'avis du SCHEER. La Commission appuie en effet sa position de statu quo en la matière sur les conclusions des récents travaux du SCHEER qui n'a pas proposé la révision des valeurs limites.

Je vous remercie de bien vouloir me transmettre votre proposition de contrat d'expertise de ces travaux dont le rendu est attendu pour le 31 décembre 2019.

P/O

Jérôme SALOMON

Destinataires en copie :

Ministère de l'économie et des finances
DGE
Bureau de la réglementation des produits

DGCCRF
Bureau des produits industriels (5A)

Ministère de la transition écologique et solidaire
DGPR
Mission Bruit et Agents Physiques