

**Evaluation of the interactions and radiation characteristics during the generation of the UV-C radiation of the UV emitter "ViraPrevent" against the background of the current state of medical knowledge and the current state of expert knowledge, respectively.**

Efficient bacterial and viral inactivation of the air in the room and of the surfaces of the equipment in it, or of the surfaces of the clothing and objects carried by the persons occupying the room, requires continuous homogeneous irradiation or homogeneous penetration of the room. As a result, the human skin, if it is not covered by clothing or similar, and the eyes form the interaction medium. In this context, the epidermis as well as the cornea, i.e., the cornea of the eye are considered as factual interaction interfaces. The following figures 1.1.1 and 1.1.2 as well as 1.2.1 and 1.2.2 show the layered structure of the human epidermis as well as the sectional view of the human eye.

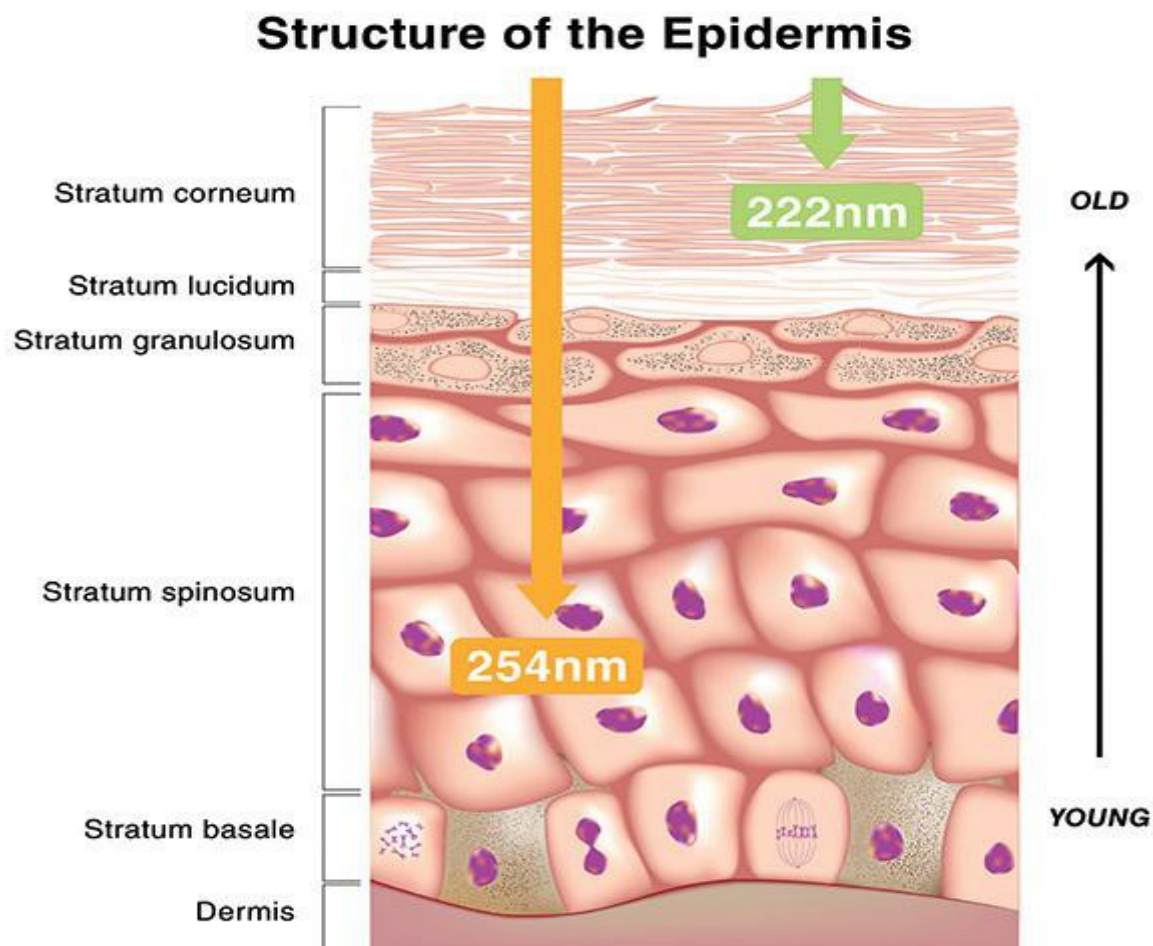


Figure 1.1.1

**Illustration of the passage depths of the UV-C wavelengths of 222 nm and 254 nm in the layer structures of the human epidermis**  
 according to "Far-UV-C Disinfection\* Modules in the Workplace: Testing Effectiveness of Long-Range Surface Disinfection" . Ushio White Paper

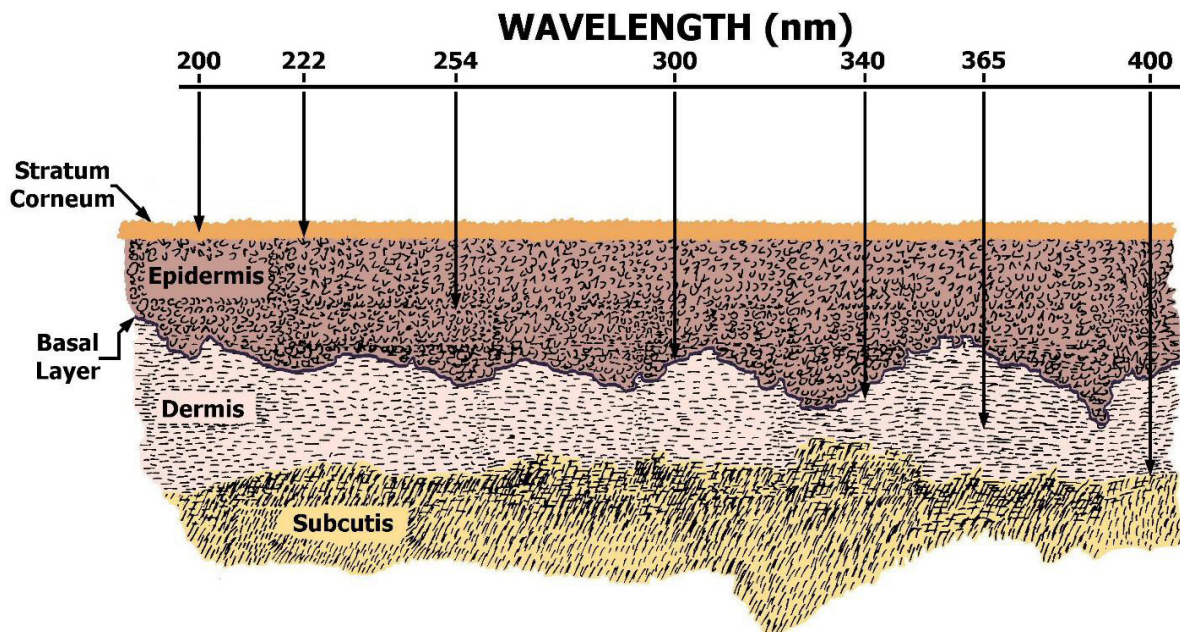


Figure 1.1.2

**Illustration of the penetration of UV wavelengths into human skin** according to "Far UV-C Radiation: Current State-of Knowledge" . White Paper of the IUVA Task Force (TF) on Far UV-C Radiation for Disinfection of Air and Surfaces

**Note :**

*The arrows indicate the wavelength-dependent absorption depth with a 90% absorption coefficient. Here it can be seen that UV-C wavelengths of 222 nm cannot penetrate the stratum corneum. On the other hand UV-C wavelengths of 254 nm penetrate the upper epidermis. UV-B wavelengths of 300 nm penetrate the germinative (basal) layer of the epidermis and generate significant DNA mutation potential due to their photon energy profile. UV-A wavelengths of 340 nm, 360 nm and 400 nm show the penetration capacity into the dermis, where the DNA mutation potential is lower than at the UV-B wavelengths of 300 nm.*

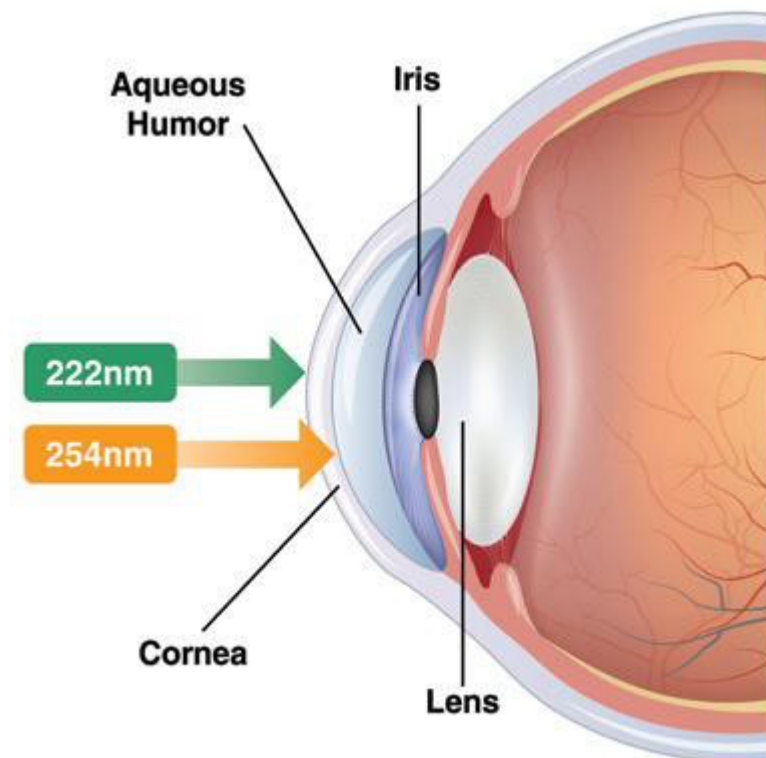


Figure 1.2.1

**Illustration of the passage depths of the UV-C wavelengths of 222nm and 254 nm in the layered structures of the human eye** according to "Far-UVC Disinfection\* Modules in the Workplace: Testing Effectiveness of Long-Range Surface Disinfection" . Ushio White Paper

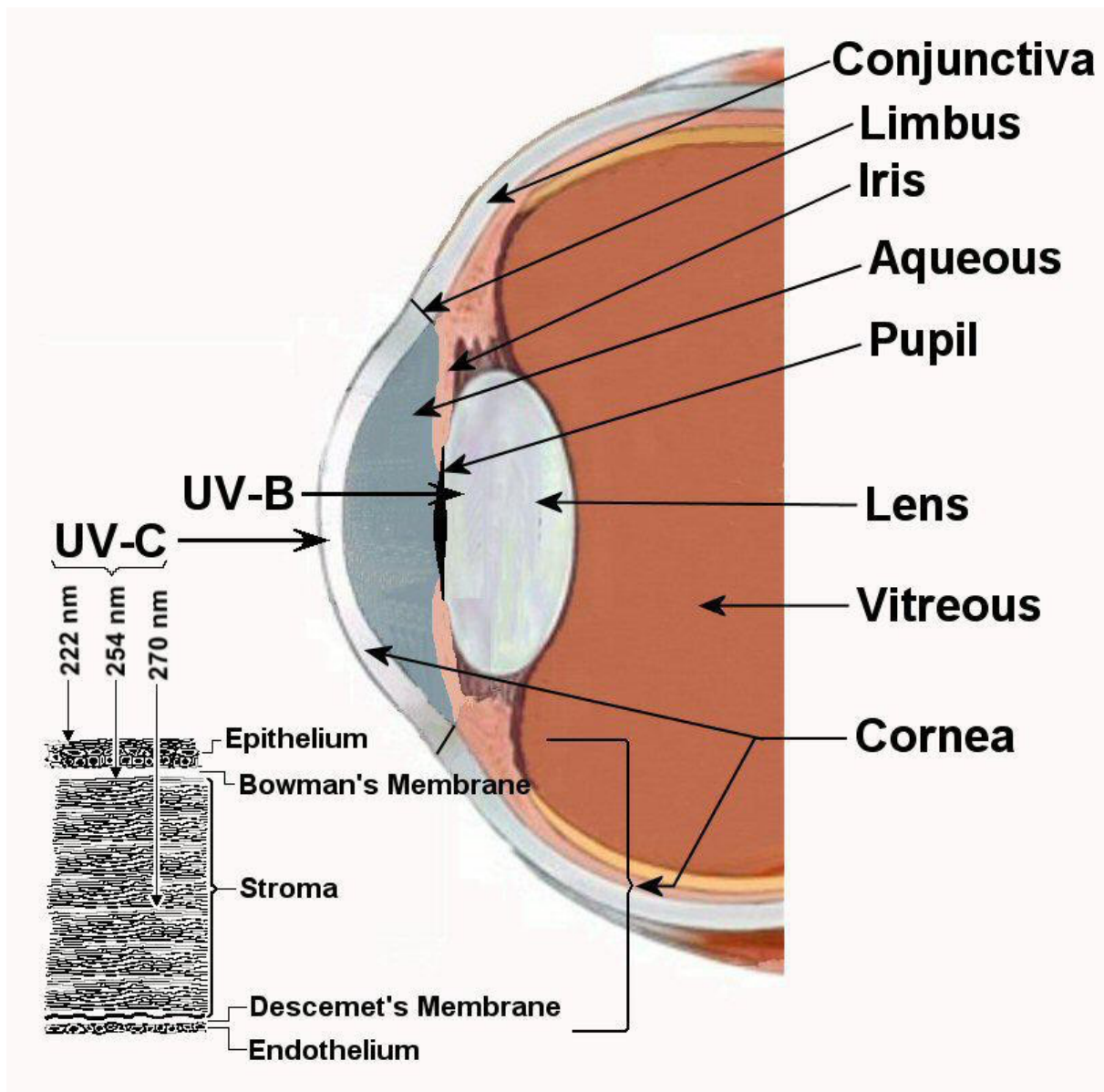


Figure 1.2.2

**Illustration of the penetration of UV wavelengths into the human eye** according to "Far UV-C Radiation: Current State-of Knowledge". White Paper of the IUVA Task Force (TF) on Far UV-C Radiation for Disinfection of Air and Surfaces

**Note :**

*The arrows indicate the wavelength-dependent penetration depth of UV radiation. It can be seen that UV-C wavelengths of 222 nm penetrate minimally into the corneal epithelium. In contrast, UV-C wavelengths of 254 nm as well as 270 nm penetrate significantly into the epithelium and into the stroma, whereas a further penetration up to the endothelium cannot be excluded. UV-B wavelengths of 300 nm show significant penetration into the lens as well as into the germinal layer of the lens behind the iris and generate a determining DNA mutation potential due to their photon energy profile. The longer wavelength UV-A radiation is highly absorbed by means of the fluorophores of the lens, so that the UV-A passage potential of the retina is significantly reduced.*

The stratum corneum is the outer layer of the epidermis and consists of dead squamous epithelial cells, the corneocytes, which have no nucleus or cell organelles. The stratum corneum forms the outer boundary of the human body to the environment. Its defense mechanisms or barriers are physical (stratum corneum and melanin), chemical (epidermal lipids and relevant enzymes), biological (symbiotic flora) and/or immunological /1/. From an illustrative point of view, the stratum corneum consists of protein-rich horny cells, the corneocytes and a lipophilic intercellular matrix in the form of an intercellular substance.

The stratum corneum not only represents a barrier, but also transmits signals (stimuli) from the outside world to the stratum basale and in this way enables the epidermis to generate a response or reaction to a signal or stimulus acting on it.

/1/ Plewig G, Jansen T, Schürer NY: *Das Stratum corneum. Hautarzt* 1997; 48: 510-521.

*Dr. med. Thomas Jansen, Dermatologische Klinik und Poliklinik, Ludwig-Maximilians-Universität, Frauenlobstraße 9-11, 80337 München.*

The effect of the UV emitter is based on the generation of UV radiation with the potential to sustainably and reliably inactivate such super pathogens as MRSA, influenza, MERS-CoV as well as deadly viruses such as the Ebola viruses. By means of inactivating UV-exposure (UV-irradiation), the instrument is created to neutralize living cells within short interaction times. UV exposure is thus an ideal alternative to chemical disinfection. The use of chemicals for disinfection is not only associated with a high degree of environmental compatibility, but also leads to the loss of effectiveness of these chemicals due to the time-dependent development of resistance of microorganisms to the chemicals used. In contrast, no known living cells exhibit resistance development potential to incident ultraviolet radiation passing through vital cellular layers. In the wavelength ranges above 230 nm, UV radiation has the ability to penetrate into the deeper layers of the epidermis and trigger molecular changes. With increasing frequency or decreasing wavelength, the penetration capacity is significantly reduced, so that the penetration of UV radiation in the wavelength ranges below 230 nm is limited exclusively to the outer skin layer. The penetration capacity of UV radiation in a wavelength range below 230 nm, here 222 nm, and in a wavelength range above 230 nm, here 254 nm and 270 nm, is illustrated comparatively in this context in Figures 1.1.1 and 1.1.2 as well as 1.2.1 and 1.2.2.

Based on this or derived from it, the wavelength range of the object energy in the form of UV radiation inducing bacterial and viral inactivation of the room air and the surfaces accessible therein is focused exclusively on the wavelength range between 190 nm and 230 nm ("remote UVC") /2/- /5/.

/2/ Welch, D., Buonanno, M., Grilj, V., Shuryak, I., Crickmore, C., Bigelow, A. W., Randers-Pehrson, G., Johnson, G. W. and Brenner, D. J. (2018)

*Far-UVC light: A new tool to control the spread of airborne-mediated microbial diseases. Sci. Rep.* 8, 1-7.

<https://doi.org/10.1038/s41598-018-21058-w>.

/3/ Kitagawa, H., Nomura, T., Nazmul, T., Keitaro, O., 146 Shigemoto, N., Sakaguchi, T. and Ohge, H. (2020)

*Effectiveness of 222-nm ultraviolet light on disinfecting SARS-CoV-2 surface contamination. Am. J. Infect. Control* 49, 299–301.

<https://doi.org/10.1016/j.ajic.2020.08.022>.

/4/ Kitagawa, H., Nomura, T., Nazmul, T., Kawano, R., Omori, K., Shigemoto, N., Sakaguchi, T. and Ohge, H. (2021)

*Effect of intermittent irradiation and fluence-response of 222 nm ultraviolet light on SARS-CoV-2 contamination. Photodiagnosis Photodyn. Ther.* 33.

<https://doi.org/10.1016/j.pdpdt.2021.102184>.

/5/ Fukui, T., Niikura, T., Oda, T., Kumabe, Y., Ohashi, H., Sasaki, M., Igarashi, T., Kunisada, M., Yamano, N., Oe, K., Matsumoto, T., Matsushita, T., Hayashi, S., Nishigori, C. and Kuroda, R. (2020)

*Exploratory clinical trial on the safety and bactericidal effect of 222-nm ultraviolet C irradiation in healthy humans. PLoS One* 15, e0235948.

<https://doi.org/10.1371/journal.pone.0235948>.

The advantage of this spectral selection to the wavelength range between 190 nm and 230 nm consists in guaranteeing the bacterial and viral inactivation potential already known and detected in the wavelength ranges between 250 nm and 280 nm, but associated with a high degree of health hazard, while at the same time excluding the health risks to be expected in these wavelength ranges /6/, /7/.

/6/ Fukui, T., Niikura, T., Oda, T., Kumabe, Y., Ohashi, H., Sasaki, M., Igarashi, T., Kunisada, M., Yamano, N., Oe, K., Matsumoto, T., Matsushita, T., Hayashi, S., Nishigori, C. and Kuroda, R. (2020)

*Exploratory clinical trial on the safety and bactericidal effect of 222-nm ultraviolet C irradiation in healthy humans. PLoS One* 15, e0235948.

<https://doi.org/10.1371/journal.pone.0235948>.

/7/ Eadie, E., Barnard, I. M. R., Ibbotson, S. H. and Wood, K. (2021)  
*Extreme Exposure to Filtered Far-UVC: A Case Study. Photochem. Photobiol.*  
<https://doi.org/10.1111/php.13385>.

Recent studies prepared and published in this regard have shown that the far UVC wavelengths hardly induce DNA damage of the skin or, in the case of induction of DNA(deoxyribonucleic acid), the induced damage is limited to the outer, non-proliferating skin cells /8/, /9/.

This limitation of induction confirms that in case of a long-term and thus also a time-continuous remote UVC exposure, the development of pathogenic changes of the skin and thus also the formation of a carcinogenic potential by induction of cyclobutane-pyrimidine dimers (CPD) or 6-4 photoproducts (6-4PP) /9/, /10/ is not to be expected.

/9/ Ikehata, H., Mori, T., Douki, T., Cadet, J. and Yamamoto, M. (2018)  
*Quantitative analysis of UV photolesions suggests that cyclobutane pyrimidine dimers produced in mouse skin by UVB are more mutagenic than those produced by UVC. Photochem. Photobiol. Sci. 17, 404 - 413.*  
<https://doi.org/10.1039/c7pp00348j>.

/10/ Barnard, I. R. M., Eadie, E. and Wood, K. (2020)  
*Further evidence that far-UVC for disinfection is unlikely to cause erythema or pre-mutagenic DNA lesions in skin. Photodermatol. Photoimmunol. Photomed. 36, 476 - 477.*  
<https://doi.org/10.1111/phpp.12580>.

## **Explanation :**

### **Cyclobutane pyrimidine dimers**

*The ultraviolet radiation component of the solar radiation spectrum, especially the high-energy UV-B wavelength range, damages the genetic material by inducing photochemical reactions between the bases of DNA. About 75% of this damage can be attributed to the so-called CPD type (CPD= cyclobutane-pyrimidine dimers). This type is caused by two neighboring pyrimidine bases (e.g. thymine bases) forming an extremely stable cyclic bond under UV-B irradiation (cyclobutane-pyrimidine dimers).*

Further recent studies /16/ - /26/ on health effects of far UV-C exposure of the eye and the skin support the findings of studies /8/, /9/ and prove the significantly lower degree of concern of far UV-C exposure in the wavelength ranges below 230 nm compared to the wavelength ranges above 230 nm.

/16/ Buonanno, M.; Ponnaiya, B.; Welch, D.; Stanislauskas, M.; Randers-Pehrson, G.; Smilenov, L.; Lowy, F. D.; Owens, D. M.; Brenner, D. J.  
*Germicidal Efficacy and Mammalian Skin Safety of 222nm-UV Light. Radiat. Res. 2017, 187 (4), 483-491.*

/17/ Buonanno, M.; Randers-Pehrson, G.; Bigelow, A. W.; Trivedi, S.; Lowy, F. D.; Spotnitz, H. M.; Hammer, S. M.; Brenner, D. J.  
207nm-UV light - a promising tool for safe low-cost reduction of surgical site infections.

*In-vitro studies. PLoS One* **2013**, 8 (10), e76968.

/18/ Buonanno, M.; Stanislauskas, M.; Ponnaiya, B.; Bigelow, A. W.; Randers-Pehrson, G.; Xu, Y.; Shuryak, I.; Smilenov, L.; Owens, D. M.; Brenner, D. J.  
207nm-UV-Light-A Promising Tool for Safe Low-Cost Reduction of Surgical Site Infections. II: In-Vivo Safety Studies.

*PLoS One* **2016**, 11 (6), e0138418.

/19/ Kaidzu, S.; Sugihara, K.; Sasaki, M.; Nishiaki, A.; Igarashi, T.; Tanito, M.  
Evaluation of acute corneal damage induced by 222nm- and 254nm-ultraviolet light in Sprague-Dawley rats.

*Free Radic Res* **2019**, 53 (6), 611-617.

/20/ Fukui, T.; Niikura, T.; Oda, T.; Kumabe, Y.; Ohashi, H.; Sasaki, M.; Igarashi, T.; Kunisada, M.; Yamano, N.; Oe, K.; Matsumoto, T.; Matsushita, T.; Hayashi, S.; Nishigori, C.; Kuroda, R.

Exploratory clinical trial on the safety and bactericidal effect of 222nm-ultraviolet C irradiation in healthy humans.

*PLoS One* **2020**, 15 (8), e0235948.

/21/ Cadet, J.

Harmless Effects of Sterilizing 222nm far-UV Radiation on Mouse Skin and Eye Tissues.

*Photochem. Photobio.* **2020**, 96 (4), 949-950.

/22/ Barnard, I. R. M.; Eadie, E.; Wood, K.

Further evidence that far-UVC for disinfection is unlikely to cause erythema or pre-mutagenic DNA lesions in skin.

*Photodermatol. Photoimmunol. Photomed.* **2020**, 36 (6), 476-477.

/23/ Hanamura, N.; Ohashi, H.; Morimoto, Y.; Igarashi, T.; Tabata, Y.

Viability evaluation of layered cell sheets after ultraviolet light irradiation of 222nm.

*Regen Ther.* **2020**, 14, 344-351.

/24/ Yamano, N.; Kunisada, M.; Kaidzu, S.; Sugihara, K.; Nishiaki-Sawada, A.; Ohashi, H.; Yoshioka, A.; Igarashi, T.; Ohira, A.; Tanito, M.; Nishigori, C.

Long-term Effects of 222nm-ultraviolet radiation C Sterilizing Lamps on Mice Susceptible to Ultraviolet Radiation.

*Photochem. Photobiol.* **2020**, 96 (4), 853-862.

/25/ Hickerson, R. P.; Conneely, M. J.; Tsutsumi, S. K. H.; Wood, K.; Jackson, D. N.; Ibbotson, S. H.; Eadie, E.

Minimal, superficial DNA damage in human skin from filtered far-ultraviolet-C (UV-C).

*Br. J. Dermatol* (2021) <https://doi.org/10.1111/bjd.19816>.

/26/ Buonnano, M.; Welch, D.; Brenner, D. J.

Exposure of human skin models to KrCl excimer lamps: The impact of optical filtering

*Photochemistry and Photobiology (2021) In Press.*

/27/ Woods, J. A.; Evans, A.; Forbes, P. D.; Coates, P. J.; Gardner, J.; Valentine, R. M.; Ibbotson, S. H.; Ferguson, J.; Fricker, C.; Moseley, H.

*The effect of 222nm-UVC phototesting on healthy volunteer skin: a pilot study. Photodermatol. Photoimmunol. Photomed. 2015, 31 (3), 159-66.*

/28/ Goldfarb, A. R.; Sidel, L. J.

*Ultraviolet absorption spectra of proteins. Science 1951, 114 (2954), 156-7.*

/29/ Setlow, J.

*The molecular basis of biological effects of ultraviolet radiation and photoreactivation. In Current topics in radiation research, M, E.; A, H., Eds. North Holland Publishing Company: Amsterdam, 1966; Vol. II, pp 195-248.*

Here, the experimental observations regarding the wavelength dependence as well as the penetration depth are in agreement with the current state of scientific knowledge /17/, /28/, /29/.

Various studies performed in the time preceding the modern studies with the focus on the evaluation of the risk potential of photocarcinogenesis concentrated exclusively on the 254nm range as well as defined UV-B and UV-A wavelength ranges /30/.

/30/ Forbes, P. D.; Cole, C. A.; Forbes, P. D.; deGrujil, F.

*Origins and Evolution of Photocarcinogenesis Action Spectra, Including Germicidal UVC. 2020.*

In this regard, recent studies by Buonanno et al.

/26/, which are based on a qualified ex vivo model of human skin (EpiDerm), focus on the correlation between radiation exposure and CPD formation for the case of defined irradiation doses. Here, the investigations lead to the conclusion that exposure of the skin to unfiltered far UV-C radiation at an irradiation dose density of up to 125 mJ/cm<sup>2</sup> does not result in significantly increased formation of premutagenic cyclobutane pyrimidine dimer(CPD) or DNA lesions. An incipient formation potential of premutagenic cyclobutane-pyrimidine dimers was observed at an irradiation dose density of 500 mJ/cm<sup>2</sup>.

These results are in agreement with the findings of Yamano et al /24/, who performed a study in hairless mice by exposing two genotypes of hairless mice with pronounced susceptibility to carcinogenesis to a far-UV-C dose density of 500 mJ/cm<sup>2</sup>. Here, the initiators of this study reported weak evidence of CPDs, but limited exclusively to the outermost cells of the epidermis. The results of other recent in vivo studies on human skin /25/ also led to this finding. In agreement with these observations Yamano et al /62/ in the results of their studies on mice with significant tendency to form skin cancer formation, Yamano et al. also ruled out far-UV-C-induced skin cancer formation.

/8/ Ewan Eadie, Paul O'Mahoney, Louise Finlayson, Isla Rose Mary Barnard, Sally Helen Ibbotson, Kenneth Wood

*Dramatically Less DNA Damage 1 from Far-UVC Krypton Chloride Lamps (222 nm)*

than from Daylight

<https://www.researchgate.net/publication/350373261>

This induction limitation confirms that in the case of long-term and thus also time-continuous remote UVC exposure, the development of pathogenic changes in the skin and thus also the formation of a carcinogenic potential by induction of cyclobutane-pyrimidine dimers (CPD) or 6-4 photoproducts (6-4PP) /9/, /10/ is not to be expected.

/9/ Ikehata, H., Mori, T., Douki, T., Cadet, J. and Yamamoto, M. (2018) *Quantitative analysis of UV photolesions suggests that cyclobutane pyrimidine dimers produced in mouse skin by UVB are more mutagenic than those produced by UVC. Photochem. Photobiol. Sci.* 17, 404 - 413.

<https://doi.org/10.1039/c7pp00348j>.

/10/ Barnard, I. R. M., Eadie, E. and Wood, K. (2020)

*Further evidence that far-UVC for disinfection is unlikely to cause erythema or pre-mutagenic DNA lesions in skin. Photodermatol. Photoimmunol. Photomed.* 36, 476 - 477.

<https://doi.org/10.1111/phpp.12580>.

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### **Cyclobutane pyrimidine dimers**

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In order to compare the exposure effect at wavelengths < 230 nm with the exposure of daylight surrounding humans, the results of Barnard et al. /10/, which are based on the site-dependent (top of epidermis, middle of epidermis, basal layer) simulation of Monte Carlo radiative transfer (MCRT) and the relative CPD generation within the layers of human skin, can be used. The determination of these values is based here on the qualification of combined MCRT models according to Barnard et al. /10/ with a five-layer human skin model under the

assumption that no melanin protection is present in the epidermis (Fitzpatrick Skin Type I) and a stratum corneum of 15 µm thickness. The data obtained on this basis allowed the determination of the relative CPD generation per incident radiation. From the evaluation of CPD generation, it was subsequently possible to determine the action spectra for CPD yield up to a wavelength of 365 nm within the skin layers considered (top of the epidermis, middle of the epidermis, basal layer) could be determined.

**Explanation :**

*CPD damage is associated with significant effects on the cell, as biochemical DNA reactions at these damage sites are abruptly halted. Unrepaired CPDs and 6-4PPs cause UV "signature mutations" that are characteristic of characteristic of carcinomas of the skin.*

The aim of this study was or is, in a narrower sense, to establish a qualified basis for the comparative assessment of occurring DNA damage as a consequence of far-ultraviolet C(far-UVC) exposure with exposure damage as a consequence of natural daylight exposure both in temperate climates (Harwell/England) and in Mediterranean climates (Thessaloniki/Greece). In order to determine the relative CPD yield of unfiltered and filtered far UVC as well as daylight, the published results of Barnard et al. /11/ were used as a basis in this context.

*/11/ Barnard, I.R.M (2020) Photodermatol. Photoimmunol. Fotomed. 36, 476-477*

Under a 10-minute daylight exposure at an ultraviolet (UV) index of 4, which can be assumed to be typical of a temperate climate from spring to fall, the same number of cyclobutane pyrimidine dimers (CPDs) are produced here as in a 750-hour exposure to unfiltered far UV-C or as in a 30,000-hour exposure to filtered far UV-C at the basal layer. At the upper boundary of the epidermis, these values reduce to 31 hours and 261 hours, respectively. Thus, it is evident that the risk potential of CPD formation due to far UV-C exposure is significantly minimal compared with the risk potential of CPD formation due to daylight exposure or, as such, should be evaluated exclusively as a theoretical risk potential.

The results presented in Table 1 show the significant difference between the minimal CPD formations produced by the 222 nm KrCl(krypton chloride) sources compared to the CPD formations produced by daylight exposure. In terms of carcinogenic risk, the basal layer should be considered a critical layer in this context. To produce the same number of CPD, using current exposure limits, a 30,000+ hour exposure using a 222 nm KrCl source correlates with a 10 minute exposure using radiation from the English sun with a UV index of 4, which is usually reached from spring to autumn /12/.

*/12/ McLellan, L. J., O'Mahoney, P., Khazova, 187 M., Higlett, M., Ibbotson, S. H. and Eadie, E. (2019)*

*Ultraviolet radiation exposure during daylight Photodynamic Therapy. Photodiagnosis Photodyn. Ther. 27, 19 - 23.*

*<https://doi.org/10.1016/j.pdpdt.2019.05.020>.*

From a scientific point of view, the computer-aided simulation models of skin layer-dependent radiation transmission on which the investigations were based are considered to be reliable. Analogous investigations of further studies /7/,/8/ and /12/ confirm these results. Here, /8-Buonanno et al./ have demonstrated the reduction of the CPD formation risk due to spectral selection mechanisms. The studies /7/ confirm the extreme minimization of the CPD formation risk even at very high dose levels of 6,000 mJcm<sup>-2</sup>.

**Table 1**

Time in hours to produce equivalent CPD to 10 minutes of daylight exposure in Thessaloniki (UV Index 8.6) and Harwell (UV Index 4.1)

	Thessaloniki		Harwell	
	Woods et al. 2015	Ushio Care222	Woods et al. 2015	Ushio Care222
Top Epidermis	57	480	31	261
Mid Epidermis	299	10,100	169	5,700
Basal Layer	1,270	51,000	750	30,300

After decades of public health warnings about the UV exposure from solar radiation, ignoring the wavelengths below 290 nm, there is an urgent need to convey the message that the exposure effects of the far-UVC wavelength range (< 230 nm) and the exposure effects due to daylight (> 230 nm) are significantly different. In this context, study /13/ particularly points out the dependence of the CPD formation on the wavelength of the irradiation.

/13/ Hickerson, (1 ) M.J. Conneely, (1) S.K. Hirata Tsutsumi, (1) K. Wood, (2) D.N. Jackson, (3) S.H. Ibbotson (4) and Eadie, (5) E.

*Minimal, superficial DNA damage in human skin from filtered far-ultraviolet-C(UV-C) British Journal of Dermatology . January 2021*

(1) Division of Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee, Dundee DD1 5E

(2) SUPA, School of Physics & Astronomy, University of St Andrews, St Andrews, KY16 9SS

(3) Department of Dermatology, Ninewells Hospital and Medical School, Dundee, DD1 9SY

(4) Scottish Photobiology Service, Photobiology Unit, University of Dundee, Ninewells Hospital and Medical School, Dundee, DD1 9SY

(5) Scottish Photobiology Service, Photobiology Unit, NHS Tayside, Ninewells Hospital and Medical School, Dundee, DD1 9SY

Here, this study was able to demonstrate in a significant manner that the exposure of the epidermis for the case of filtered remote UV-C exposure lacks an observable CPD formation within the basal layer of the epidermis. As the single-layer innermost cell layer of the epidermis, the basal cell layer serves to regenerate the skin. The basal cell layer is hereby the functional carrier of cell division, due to which its response or sensitivity to UV-C exposure is associated with significant significance.

On the basis of the analysis of the UV-exposed skin samples the CPD formation within the epidermis of two subjects for the test and exposure cases, respectively :

1. narrow-band UV-B exposure
2. spectral selective far UV-C exposure

investigated. As a result of the exposure, the evaluation of histological staining of both ex vivo and irradiated in vivo skin of the two test subjects was performed.

As expected, significant CPD formation was observed throughout the epidermis of the ex vivo skin sample, whose ex vivo control sample was shown to be CPD negative, after narrowband UV-B irradiation.

Both ex-vivo and in-vivo filtered remote UV-C exposure of the human skin samples resulted in minimal CPD formation, but this was confined to the upper layers of the epidermis without any effect on the basal layer. In this regard, the control in vivo specimens from the subjects were demonstrably CPD negative.

### **Ocular exposure**

The effects of ocular exposure to far-UV-C wavelengths have been the subject of very few studies. Kaidzu et al. /19/, /31/ assessed threshold photokeratitis based on a rat eye model. Using slit-lamp biomicroscopy, the studies focused on the examination or assessment of staining and surface mapping. The initiators of the studies reported exposure thresholds at UV-C wavelengths of 207 nm, 222 nm, 235 nm, and 254 nm, and at a UV-B wavelength of 311 nm. Here, detectable effects on the cornea of rat eye models observed at the wavelengths of 207 nm and 222 nm, for radiation dose densities exceeding 5,000 mJ/cm<sup>2</sup> and 15,000 mJ/cm<sup>2</sup>, respectively. Kaidzu et al. /19/, /31/ also undertook a histological assessment of the cornea in this context using CPDs as markers of DNA damage. The analysis was performed as a function of wavelength as a function of exposure dose. Here, the depth of the observed CPDs varied as a function of wavelength, although for the case of the far-UV-C exposures at 207 nm and 222 nm, CPD formation was limited exclusively to the superficial cells of the corneal epithelium, i.e., the cells that are shed within a few days within the regular life cycle of the corneal epithelium. Penetration of the germ cell layer was not observed for the case of far UV-C exposures at the wavelengths of 207 nm and of 222 nm. Analogous to the epidermis, the germ cells of the cornea are located in the limbus, i.e., in the border area between the cornea as well as the conjunctiva and thus in an area protected from the far UV-C radiation by several upstream cell layers /14/.

For the case of 254 nm irradiations as well as 313 nm irradiations, CPDs were observed in all layers of the cornea including the corneal endothelium.

/31/ Kaidzu, S.; Sugihara, K.; Sasaki, M.; Nishiakiba, A.; Ohashi, H.; Igarashi, T.; Tanito, M.

*Re-evaluation of rat corneal damage by short wavelength UV revealed extremely less hazardous property of 222 nm-UV-C.*

*Private Communication, Under Peer Review 2021.*

/14/ Rich. M. Simons

*Far UV-C in the 200 - 225nm range, and its potential for disinfection applications*  
IUAV International Ultraviolet Association, July 2020

/15/ Far UV-C Radiation: Current State of Knowledge

*White Paper 2021 der IUVA Task Force (TF) on Far UV-C Radiation for Disinfection of Air and Surfaces*

**Expert evaluation :**

Guidelines for human UV-C radiation exposure are currently identical worldwide. The leading bodies for the preparation of guidelines, whose limit value surveys or limit value publications during the past three decades are to be regarded as unchanged and valid /32/,/33/, are the ACGIH American Conference of Governmental Industrial Hygienists and the ICNIRP International Commission on Non-Ionizing Radiation Protection.

*/32/ ACGIH 2021*

*TLVs and BEIs: Based on the Documentation of the Threshold Limit Values for Chemical and Physical Agents & Biological Exposure Indices; American Conference of Governmental Industrial Hygienists: Cincinnati, OH, 2021.*

*/33/ ICNIRP*

*Guidelines on limits of exposure to ultraviolet radiation of wavelengths between 180 nm and 400 nm (incoherent optical radiation). Health Physics **2004**, 87 (2), 171-186.*

Based on the exposure limits established by the ICNIRP International Committee on Non-Ionizing Radiation Protection, the ACGIH American Conference of Governmental Industrial Hygienists, the EC European Commission, the ANSI/IEC American National Standards Institute/Illuminating Engineering Society, and the CEI/IEC International Electrotechnical Commission, a wavelength-dependent 8-hour equivalent of the exposure limits for the assessment of the permissible radiation dose density of the product UV emitter "ViraPrevent" can be calculated.

"ViraPrevent" within the wavelength range between 190 nm and 230 nm. As an update and supplement, the American Conference of Governmental Industrial Hygienists published a "Notice of Intended Change" of the UV limit values (TLVs), on the basis of which an organ-specific tailoring of the limit value conditions with the respective separated scope for the UV radiation exposure of the skin as well as the UV radiation exposure of the eye and, consequently, the collection of both skin- and eye-specific limit values for the wavelength range below 300 nm took place. In this context, the increase of the current limit values for the case of UV radiation exposure of the eye in the wavelength ranges below the wavelength of 250 nm /32/ was carried out.

Based on the "Notice of Intended Change" published by the ACGIH of the UV limits (TLVs) for the UV-C wavelength range published by the ACGIH, the 8-hour exposure limits listed below can be identified :

EYES	SKIN
190 nm : 1050 mJ/cm <sup>2</sup>	10100 mJ/cm <sup>2</sup>
200 nm : 1050 mJ/cm <sup>2</sup>	10100 mJ/cm <sup>2</sup>
210 nm : 1050 mJ/cm <sup>2</sup>	2000 mJ/cm <sup>2</sup>

220 nm :	230 mJ/cm <sup>2</sup>	1050 mJ/cm <sup>2</sup>
230 nm :	110 mJ/cm <sup>2</sup>	210 mJ/cm <sup>2</sup>

Both animal and human histological studies show that possible DNA damage as a consequence of remote UV-C exposure occurs only in the outer layer of the epidermis in the form of a squamous epithelial layer consisting of non-vital cells. In this respect, the interaction of far UV-C radiation with human or animal skin is limited to the outer layer of the skin, which consists exclusively of non-vital cells and thus the basis of the development or formation of pathogenic, in particular carcinogenic changes per se is not given. The vulnerable basement membrane, which separates the epidermis from the dermis and from which the carcinogenic risk potential of health concern arises, i.e. from which the majority susceptibility for skin tumor formation, remains unaffected and intact.

The simulation of the far UV-C irradiation on the basis of the modeling of the layer model of the epidermis assumes an average layer thickness in each case, the actual extent of which is accompanied by a significant range of variation depending on the skin type. The material composition of the skin layers is represented and taken into account by means of the respective complex susceptibility profile, which is also subject to a skin type-dependent range of variation. The modeling results obtained from the transmission simulation allow quantification of the degree of reduction of the radiation intensity on the transmission path within the squamous epithelial layer. Here, the evaluation of the transmittance is accompanied by the need to define or determine the radiation intensity of far-UV-C radiation both as it enters the squamous epithelial layer and as it exits the squamous epithelial layer. The radiation intensity observable at the exit from the squamous epithelial layer, which in this form constitutes the input radiation component of the UV-C radiation acting on the inner layers of the epidermis, represents the determining parameter of the pathogenic risk assessment in this context. For the passage of the squamous epithelial layer, an average transmittance of the irradiated far UV-C radiation of 0.07 can be assumed. In this respect, the associated or quantified transmittance ratio enables the definition of the radiation intensity or, further, also the radiation dose and/or radiation dose density, on the basis of which a far UV-C radiation impinging on the surface of the epidermis can be assessed with regard to the associated pathogenic consequences. associated pathogenic consequences can be assumed to be harmless.

The wavelength ranges of the ultraviolet radiation spectrum used as a basis for bacterial and viral inactivation ensure the sustainable and reliable inactivation of the room air of closed and/or semi-closed rooms as well as the surfaces of the fixed and/or portable equipment located therein, the clothing of the persons occupying the room as well as the skin surfaces of the people and animals occupying the room. Under the conditions of time-discrete or time-continuous operation of the UV emitter in question, bacterial and viral inactivation takes place without the risk of revitalization of the inactivation objects and without any potential health hazard for humans and animals due to exposure to ultraviolet light within the wavelength range between 190 nm and 230 nm.