CIE

COMMISSION INTERNATIONALE DE L'ECLAIRAGE
INTERNATIONAL COMMISSION ON ILLUMINATION
INTERNATIONALE BELEUCHTUNGSKOMMISSION

TECHNICAL REPORT

UV-C PHOTOCARCINOGENESIS RISKS FROM GERMICIDAL LAMPS

CIE 187:2010

THE INTERNATIONAL COMMISSION ON ILLUMINATION

The International Commission on Illumination (CIE) is an organisation devoted to international co-operation and exchange of information among its member countries on all matters relating to the art and science of lighting. Its membership consists of the National Committees in about 40 countries.

The objectives of the CIE are:
1. To provide an international forum for the discussion of all matters relating to the science, technology and art in the fields of light and lighting and for the interchange of information in these fields between countries.
2. To develop basic standards and procedures of metrology in the fields of light and lighting.
3. To provide guidance in the application of principles and procedures in the development of international and national standards in the fields of light and lighting.
4. To prepare and publish standards, reports and other publications concerned with all matters relating to the science, technology and art in the fields of light and lighting.
5. To maintain liaison and technical interaction with other international organisations concerned with matters related to the science, technology, standardisation and art in the fields of light and lighting.

The work of the CIE is carried on by seven Divisions each with about 20 Technical Committees. This work covers subjects ranging from fundamental matters to all types of lighting applications. The standards and technical reports developed by these international Divisions of the CIE are accepted throughout the world.

A plenary session is held every four years at which the work of the Divisions and Technical Committees is reviewed, reported and plans are made for the future. The CIE is recognised as the authority on all aspects of light and lighting. As such it occupies an important position among international organisations.

LA COMMISSION INTERNATIONALE DE L'ECLAIRAGE

La Commission Internationale de l'Eclairage (CIE) est une organisation qui se donne pour but la coopération internationale et l'échange d'informations entre les Pays membres sur toutes les questions relatives à l'art et à la science de l'éclairage. Elle est composée de Comités Nationaux représentant environ 40 pays.

Les objectifs de la CIE sont :
1. De constituer un centre d'étude international pour toute matière relevant de la science, de la technologie et de l'art de la lumière et de l'éclairage et pour l'échange entre pays d'informations dans ces domaines.
2. D'élaborer des normes et des méthodes de base pour la métrologie dans les domaines de la lumière et de l'éclairage.
3. De donner des directives pour l'application des principes et des méthodes d'élaboration de normes internationales et nationales dans les domaines de la lumière et de l'éclairage.
4. De préparer et publier des normes, rapports et autres textes, concernant toutes matières relatives à la science, la technologie et l'art dans les domaines de la lumière et de l'éclairage.
5. De maintenir une liaison et une collaboration technique avec les autres organisations internationales concernées par des sujets relatifs à la science, la technologie, la normalisation et l'art dans les domaines de la lumière et de l'éclairage.

Les travaux de la CIE sont effectués par 7 Divisions, ayant chacune environ 20 Comités Techniques. Les sujets d'études s'étendent des questions fondamentales, à tous les types d'applications de l'éclairage. Les normes et les rapports techniques élaborés par ces Divisions Internationales de la CIE sont reconnus dans le monde entier.

Tous les quatre ans, une Session plénière passe en revue le travail des Divisions et des Comités Techniques, en fait rapport et établit les projets de travaux pour l'avenir. La CIE est reconnue comme la plus haute autorité en ce qui concerne tous les aspects de la lumière et de l'éclairage. Elle occupe comme telle une position importante parmi les organisations internationales.

DIE INTERNATIONALE BELEUCHTUNGSKOMMISSION

Die Internationale Beleuchtungskommission (CIE) ist eine Organisation, die sich der internationalen Zusammenarbeit und dem Austausch von Informationen zwischen ihren Mitgliedsländern bezüglich der Kunst und Wissenschaft der Lichttechnik widmet. Die Mitgliedschaft besteht aus den Nationalen Komitees in rund 40 Ländern.

Die Ziele der CIE sind :
1. Ein internationaler Mittelpunkt für Diskussionen aller Fragen auf dem Gebiet der Wissenschaft, Technik und Kunst der Lichttechnik und für den Informationsaustausch auf diesen Gebieten zwischen den einzelnen Ländern zu sein.
2. Grundnormen und Verfahren der Messtechnik auf dem Gebiet der Lichttechnik zu entwickeln.
3. Richtlinien für die Anwendung von Prinzipien und Vorgängen in der Entwicklung internationaler und nationaler Normen auf dem Gebiet der Lichttechnik zu erstellen.
4. Normen, Berichte und andere Publikationen zu erstellen und zu veröffentlichen, die alle Fragen auf dem Gebiet der Wissenschaft, Technik und Kunst der Lichttechnik betreffen.
5. Liaison und technische Zusammenarbeit mit anderen internationalen Organisationen zu unterhalten, die mit Fragen der Wissenschaft, Technik, Normung und Kunst auf dem Gebiet der Lichttechnik zu tun haben.

Die Arbeit der CIE wird in 7 Divisionen, jede mit etwa 20 Technischen Komitees, geleistet. Diese Arbeit betrifft Gebiete mit grundlegendem Inhalt bis zu allen Arten der Lichtanwendung. Die Normen und Technischen Berichte, die von diesen international zusammengesetzten Divisionen ausgearbeitet werden, sind von der ganzen Welt anerkannt.

Alle vier Jahre findet eine Session statt, in der die Arbeiten der Divisionen überprüft, berichtet und neue Pläne für die Zukunft ausgearbeitet werden. Die CIE wird als höchste Autorität für alle Aspekte des Lichtes und der Beleuchtung angesehen. Auf diese Weise unterhält sie eine bedeutende Stellung unter den internationalen Organisationen.

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UV-C PHOTOCARCINOGENESIS RISKS FROM GERMICIDAL LAMPS

CIE 187:2010

This Technical Report has been prepared by CIE Technical Committee 6-59 of Division 6 "Photobiology and Photochemistry" and has been approved by the Board of Administration of the Commission Internationale de l'Eclairage for study and application. The document reports on current knowledge and experience within the specific field of light and lighting described, and is intended to be used by the CIE membership and other interested parties. It should be noted, however, that the status of this document is advisory and not mandatory. The latest CIE proceedings or CIE NEWS should be consulted regarding possible subsequent amendments.

Ce rapport technique a été élaboré par le Comité Technique CIE 6-59 de la Division 6 "Photobiologie et Photochimie" et a été approuvé par le Bureau de la Commission Internationale de l'Eclairage, pour étude et emploi. Le document expose les connaissances et l'expérience actuelles dans le domaine particulier de la lumière et de l'éclairage décrit ici. Il est destiné à être utilisé par les membres de la CIE et par tous les intéressés. Il faut cependant noter que ce document est indicatif et non obligatoire. Il faut consulter les plus récents comptes rendus de la CIE, ou le CIE NEWS, en ce qui concerne des amendements nouveaux éventuels.

Dieser Technische Bericht wurde vom Technischen Komitee CIE 6-59 der Division 6 "Photobiologie und Photochemie" ausgearbeitet und vom Vorstand der Commission Internationale de l'Eclairage gebilligt worden. Das Dokument berichtet über den derzeitigen Stand des Wissens und Erfahrung in dem behandelten Gebiet von Licht und Beleuchtung; es ist zur Verwendung durch CIE-Mitglieder und durch andere Interessierte bestimmt. Es sollte jedoch beachtet werden, dass das Dokument eine Empfehlung und keine Vorschrift ist. Die neuesten CIE-Tagungsberichte oder die CIE NEWS sollten im Hinblick auf mögliche spätere Änderungen zu Rate gezogen werden.

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The following members and advisors of TC 6-59, "UV-C Photocarcinogenesis Risks from Germicidal Lamps", took part in the preparation of this Technical Report. The committee comes under Division 6 "Photobiology and Photochemistry".

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CONTENTS

UV-C PHOTOCARCINOGENESIS RISKS FROM GERMICIDAL LAMPS

SUMMARY

Increasingly, UV-C (100 nm – 280 nm) mediated air disinfection (principally 254 nm radiant energy from low-pressure mercury lamps) is being used as a building environmental control to provide human protection from transmission of airborne pathogens such as tuberculosis bacteria, influenza viruses and other aerosolized agents. Some uses of UV-C energy require direct exposure of the volume room air in a horizontal plane directly above the heads of occupants. In these settings there is the potential of reflected or scattered UV-C radiation that could result in human exposure. Known side effects of overexposure to UV-C radiation include transient corneal and conjunctival irritation (photo-keratoconjunctivitis) and skin irritation (erythema), which disappear within a 24 – 48 hour period, not currently known to produce lasting biological damage. The ACGIH and ICNIRP threshold limit for 8 hour continuous exposure to UV-C radiation at 254 nm is 6 mJ·cm^{-2} (60 J·m^{-2}), and proper installation of well engineered UV-C systems meet this criteria. However, there have been incidents of poor installations resulting in accidental UV-C overexposures. General statements that all UVR is carcinogenic have raised safety concerns of open air UV-C systems. Although, from basic biophysical principles, UV-C radiation is carcinogenic for the same reason that it is an effective germicidal agent, the attenuation provided by the stratum corneum and epithelial tissues of the skin greatly reduces the risk relative to UV-B radiation. UV germicidal irradiation can be safely and effectively used for upper air disinfection without a significant risk for long term delayed effects such as skin cancer.

RISQUES DE PHOTOCARCINOGENESE UVC DES LAMPES GERMICIDES

RESUME

La désinfection de l'air par les UVC (100 nm – 280 nm) dont l'énergie radiante est principalement représentée par la raie 254 nm des sources mercure à basse pression, est en constante augmentation. Cette technologie est utilisée dans le contrôle de l'environnement des bâtiments afin d'assurer la protection humaine contre la transmission d'agents pathogènes transportés par l'air tels que les bactéries tuberculeuses, les virus grippaux et tout autres agents présents sous forme d'aérosols. Certaines utilisations de l'énergie UVC nécessitent une exposition directe du volume d'air d'une pièce dans un plan horizontal situé directement au-dessus de la tête des occupants. Dans ces configurations existent potentiellement des radiations UVC réfléchies ou difractées qui pourraient conduire à une exposition humaine. Les effets reconnus des surexpositions au rayonnement UVC sont essentiellement constitués d'une irritation cornéenne et conjonctivale (photo-kératoconjonctivite) et une irritation cutanée (érythème) qui disparaissent en 24 – 48 heures, et ne produisent pas de dommages biologiques retardés dans l'état des connaissances actuelles. L'ACGIH et l'ICNIRP ont défini des valeurs seuils limites pour 8 heures d'expositions continues aux UVC à 254 nm, soit 6 mJ·cm^{-2} (60 J·m^{-2}), et l'installation correcte de systèmes produisant des UVC doit remplir ces critères. Néanmoins, on a rapporté des incidents concernant de mauvaises installations produisant des surexpositions UVC accidentelles. Bien que, sur la base de principes biophysiques, le rayonnement UVC soit carcinogène pour la même raison qu'il est un agent germicide efficace, l'atténuation de ce rayonnement par l'absorption dans le stratum corneum et par les tissus épithéliaux de la peau réduit de manière importante le risque relatif du rayonnement UVB et UVC. Le rayonnement germicide UV peut être efficacement utilisé en toute sécurité pour la désinfection de l'air, sans risque significatif d'effets retardés à long terme tels que les cancers cutanés.

UV-C PHOTOKARZINOGENESE-RISIKEN DURCH KEIMTÖTENDE LAMPEN

ZUSAMMENFASSUNG

In zunehmendem Maße wird Luftdesinfektion durch UV-C (100 nm – 280 nm) (vornehmlich 254 nm Strahlungsenergie von Niederdruck-Quecksilberlampen) zur Gebäudeumweltkontrolle verwendet, um für den Schutz des Menschen vor luftübertragenen Krankheitserregern wie z.B. Tuberkulosebakterien, Grippeviren und anderen aerosolisierten Erregern zu sorgen. Einige Anwendungen von UV-C-Energie erfordern eine direkte Bestrahlung des Raumluftvolumens in einer horizontalen Ebene direkt über den Köpfen der Raumbenutzer. Bei solchen Anlagen besteht die Möglichkeit, dass reflektierte oder gestreute UV-C-Strahlung zu einer menschlichen Gefährdung führen könnte. Bekannte Nebeneffekte, die durch zu starke UV-C-Bestrahlung entstehen, sind z.B. transiente korneale and konjunktive Irritation (Photo-Keratokonjunktivitis) und Hautirritation (Erythem), welche innerhalb von 24 – 48 Stunden verschwinden, und nach bisherigen Erkenntnissen keinen dauerhaften biologischen Schaden verursachen. Die von ACGIH und ICNIRP festgelegte Schwellwertgrenze für 8 Stunden dauerhaften Aufenthalt unter UV-C-Strahlung bei 254 nm beträgt 6 mJ·cm^{-2} (60 J·m^{-2}), und eine sorgfältige Installation von fachmännisch ausgeführten UV-C-Systemen erfüllen dieses Kriterium. Dennoch gab es durch schlechte Installationen hervorgerufene Vorfälle, bei denen es zu unbeabsichtigten UV-C-Überdosierungen kam. Allgemeine Aussagen, dass jegliche UV-Strahlung karzinogen sei, haben Sicherheitsbedenken hinsichtlich der Verwendung von offenen UV-C-Systemen hervorgerufen. Obwohl aus Sicht grundlegender biophysikalischer Grundsätze UV-C-Strahlung aus demselben Grund einerseits karzinogen, andererseits aber auch ein effektiver germizider Wirkstoff ist, reduziert die Schwächung durch die Hornhautschicht und das Epithelgewebe der Haut weitgehend das Risiko relativ zur UV-B-Strahlung. Keimtötende UV-Bestrahlung kann sicher und effektiv zur Luftdesinfektion im oberen Raumbereich verwendet werden ohne signifikantes Risiko hinsichtlich Langzeiteffekten wie z.B. Hautkrebs.

1 INTRODUCTION

For over three decades, occupational health and safety officials have provided guidance on worker exposure to ultraviolet radiation [1]. With the increasing interest in the use of 254 nm radiation from low-pressure mercury lamps to reduce the risk of airborne transmission of bioaerosols, tuberculosis bacteria, influenza viruses and other infectious diseases, questions of human safety have arisen [2]. The traditional germicidal lamp is a low-pressure mercury discharge lamp with a quartz or UV-C transmitting glass envelope. Other types of germicidal lamps with broad spectral emissions are not included in the scope of this report. Figure 1 shows a typical spectral power distribution of a UV-C low-pressure mercury discharge lamp.

Overexposure to UV-C (100 nm – 280 nm) radiation can result in transient corneal irritation (photokeratitis), conjunctival irritation (photoconjunctivitis) and skin irritation (erythema), which disappear within a 24 – 48 hour period, considered to be without lasting biological damage. Although UV-C radiation kills the superficial epithelial cells of the cornea and conjunctiva, these cells are sloughed off and replaced by underlying cells within 24 hours [3]. Guidance for occupational exposure to UVR, including UV-C radiation, has been provided by the American Conference of Industrial Hygienists (ACGIH) and the International Commission on Non-Ionizing Radiation Protection (ICNIRP). These organisations have established exposure guidelines (termed "Threshold Limit Values," or TLVs[®] by ACGIH) within an 8 h interval (either continuous or intermittent exposure), and the TLV for UV-C radiation at 254 nm is 6 mJ·cm^{-2} (60 J·m^{-2}) (3 mJ·cm^{-2} (30 J·m^{-2}) effective) [1, 4]. General statements that all UVR is carcinogenic have raised safety concerns. Because of its high genotoxic potential in unprotected cells, UV-C radiation has often been presumed to be the most potent carcinogen of all UVR. However, this is a misconception based upon a lack of appreciation of the very shallow penetration depth of 254 nm radiation in human skin. Today it is considered that UV-C radiation, if appreciably carcinogenic at all, is far less carcinogenic to humans than solar UV-B radiation. This report reviews the scientific knowledge on this subject.
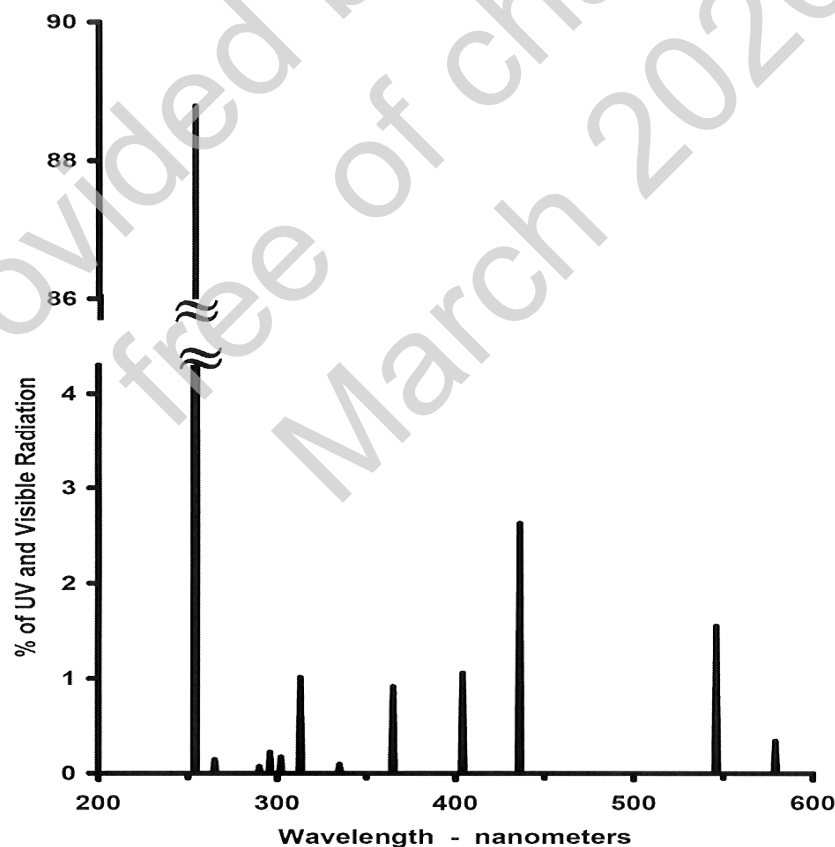

Figure 1. Spectral power distribution of a typical low-pressure mercury UV-C lamp at 1 nm resolution. Source: R. E. Levin.

2 SCOPE

To prepare a technical report on the potential carcinogenic risk of 254 nm UV-C radiation emitted from low-pressure mercury discharge lamp systems used for germicidal purposes.

3 REVIEW OF SCIENTIFIC EVIDENCE

3.1 Human Studies

Over time, humans have lived in different environmental settings with continuous environmental exposures to the ultraviolet radiation in sunlight, which contains some UV-B radiation and proportionally far more UV-A radiation. The relative levels of exposure vary greatly with geographical location. The atmosphere blocks UVR below ~ 292 nm; hence, UV-C (100 nm – 280 nm) wavelengths are not present in terrestrial solar radiation. Nevertheless, the molecular repair mechanisms which characterise UV-B defences are also effective against UV-C damage, certainly when considering DNA damage [5]. Although these particular defences are best known and understood for the spectral regions that have been exhaustively clinically studied, these DNA repair functions are known to exist for exposures at wavelengths less than 292 nm. Despite the lack of UV-C radiation in terrestrial solar radiation, many fundamental studies of DNA repair employed the 254 nm emission line of low-pressure mercury lamps. Further, although animal experimental studies show that UV-C can be carcinogenic in mice, CIE TC 6-32 corrected the relative photocarcinogenic action spectrum to take into account the much greater attenuation in human skin compared to mouse skin [3], and only trace amounts of 254 nm UV-C radiation reach the critical germinative (basal) layer of the epidermis. 254 nm radiation can elicit a minimal erythema at relatively low exposure doses, although the erythema associated with 254 nm radiation differs from the erythema associated with UV-B exposures in the following ways: (1) it is more transient; (2) it is anatomically more superficial; and (3) even at high exposure doses, it does not result in a severe sunburn. These differences are shown for various UV wavelengths in Figures 2 and 3, where Figure 2 shows the time course of erythema and Figure 3 plots the severity of erythema with increasing dose.
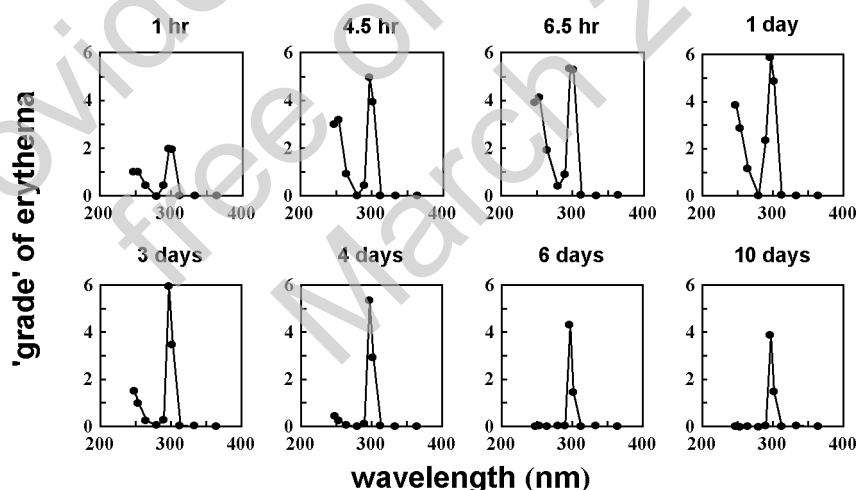

Figure 2. Classic Figure from Hausser and Vahle [6, 8] illustrating the time course of erythema for various wavelengths. Figure adapted from Sliney and Wolbarsht [7]. Hausser and Vahle used a quartz monochromator and a mercury lamp to irradiate the skin of various subjects with different wavelengths of UV radiation. The Figure shows the degree of severity of erythema as a function of wavelength, for various times after exposure. As shown, while the most severe erythemas were present at two maxima at 254 nm and 297 nm within 1 day after the exposure, the erythema and pigmentation changes caused by the short-wavelength UV-C radiation were more transient and faded within several days compared to that induced by UV-B radiation. This is due to the much more superficial penetration depth of UV-C radiation.

The studies that relate to human exposure to UV-C radiation are limited to studies of human erythema. The classic studies of Hausser and Vahle [8] showed that with increasing doses of 254 nm radiation above 1 minimal erythema dose (MED), the level of redness hardly increased - even at doses 10-fold above the exposure associated with the just-perceptible redness. This was in sharp contrast to the rapid increase in redness with 313 nm irradiation (UV-B), where severe erythema and blistering occurred at doses only 20 % above those resulting in just perceptible erythema, as shown in Figure 3. This has been interpreted to be related to the penetration depth of the UVR. From these observations, some photodermatologists (e.g., Urbach, 1999 [See Appendix 1]) have argued that UV skin carcinogenesis is not a realistic risk from germicidal lamps, since only a very small amount of radiation from the 254 nm line (that comprises over 90 % of the radiation from a low-pressure mercury discharge lamp) reaches the germinative layer of the epidermis.

Figure 2 is based on the classic work by Hausser and Vahle [6], where emissions from a mercury lamp were passed through a quartz prism monochromator and the isolated spectral emission lines (at 248 nm, 254 nm, 265 nm, 289 nm, 297 nm, 302 nm, 313 nm, 334 nm, and 365 nm) irradiated the skin of various subjects. They found that the UV-C-induced erythemas were significantly more transient than those induced by UV-B radiation.
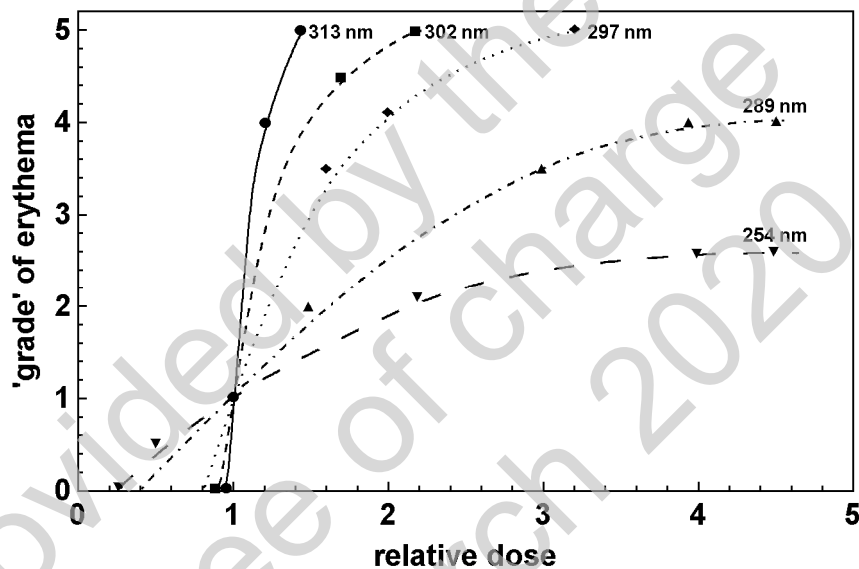

Figure 3. Relative degree or "grade" of erythema as a function of the relative dose for various ultraviolet wavelengths. Based on Hausser and Vahle [9] and adapted from Sliney and Wolbarsht [7].

3.2 Laboratory Studies

Although experimental studies in animal models demonstrate that tumours are readily produced from UV-B exposures, this is not the case for UV-C exposures. Relatively high doses of UV-C radiation were required to produce tumours in rodent models. Sterenborg [10-16] succeeded in producing skin cancers in three groups of mice, using three different daily exposure doses from low-pressure mercury germicidal lamps. The dose-effect relationship was markedly flatter than with UV-B (and UV-A) irradiation. This latter result suggests that the effect was not caused by the fraction of UV-B or UV-A in the germicidal lamp spectrum [17].

The International Agency for Research on Cancer (IARC) states that "UV-C radiation induces DNA damage in and is mutagenic to prokaryotes, fungi and chromatid exchange in amphibian and avian cells *in vitro*; it is mutagenic to and induces DNA damage, chromosomal aberrations, sister chromatid exchanges and transformation in mammalian and human cells *in vitro;* and it induces DNA damage in mammalian skin cells irradiated *in vivo.*"

Further in its evaluation, IARC states that there is *inadequate evidence* in humans for carcinogenicity of exposure to fluorescent lighting. There is *inadequate evidence* in humans

for carcinogenicity of other sources of artificial ultraviolet radiation. There is *sufficient evidence* for the carcinogenicity of ultraviolet C radiation in experimental animals. IARC's overall evaluation on UV-C radiation is that it is *probably carcinogenic to humans* (Group 2A)[1]

3.3 CIE Skin Carcinogenesis Action Spectrum

CIE TC 6-32 prepared an action spectrum for non-melanoma skin cancer, and this was published as ISO 28077:2006(E)/CIE S 019/E:2006 [3]. There was one spectral data point at 254 nm from mouse studies that was adjusted to account for the spectral transmission of the stratum corneum of human skin. However, it was emphasized that the 254 nm point is an outlier in that the dose-response differed from that in the UV-B region, i.e. the relative effectiveness of UV-C vs. UV-B may shift with dose levels.

3.4 UV-C Spectral Transmittance of the Stratum Corneum and Epidermis

The spectral transmittance of the skin has been studied for decades, with some variation in the resulting values for different layers.

There have been numerous studies over the past approximately 80 years that have examined the reflection of UV radiation off the surface of skin and the transmission of UV radiation through the stratum corneum, epidermis, and dermis. This section provides a few representative studies that have been published on the transmission of UV radiation into and through the epidermis.

If considering the carcinogenicity of a light source as the measure of biological impact, as opposed to the induction of erythema or oedema, then the critical component of the analysis is how much UV-B and UV-C radiation is reaching the border between the epidermis and dermis. It is suggested that UV induced squamous and basal cell carcinomas arise at the basement membrane separating the epidermis and dermis. As a result, a consideration of the spectral dependence of the transmission of UV radiation through the epidermis will provide an indication of the possibility that a given wavelength will induce a biological event at the basement membrane.

Reflectance of surface of stratum corneum

The first consideration is the reflection of radiation from the surface of human stratum corneum. There are several publications on this subject; however, this report examines the results presented by Diffey [18] which conclude that ultraviolet radiation (250 nm – 400 nm) scattering at the surface of human stratum corneum is essentially independent of the wavelength, as shown in Figure 4.

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1 DEFINITION OF GROUP 2A From IARC Page 35 Group 2A [17] --The agent (mixture) is probably carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans. This category is used when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent (mixture) may be classified in this category when there is inadequate evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent, mixture or exposure circumstance may be classified in this category solely on the basis of limited evidence of carcinogenicity in humans.
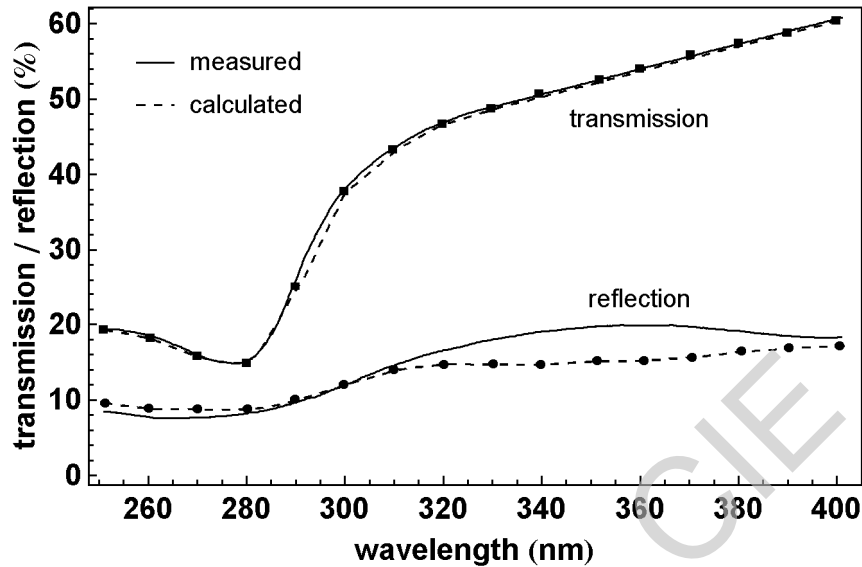
Figure 4. Spectral transmission and reflection of ultraviolet radiation in human stratum corneum. Adapted from Diffey [15].

This is in agreement with the results reported by Everett [19] where the amount of ultraviolet radiation reflected from the surface of various samples of human stratum corneum was determined. Anderson and Parrish [20] summarized several studies to conclude that the reflectance of the surface of skin is "… always between 4 % and 7 % over the entire spectrum from 250 nm – 3000 nm for both white and black skin", confirming the wavelength independent nature, but with a slightly lower value.

<u>Transmission of ultraviolet radiation through epidermis</u>

The transmission of radiation through several samples of human epidermis measured by Everett et al. [19] is shown in Figure 5 which shows the percent of transmitted radiation drops considerably below 300 nm. This reduction in transmission suggests that approximately 10-fold less radiation penetrates the epidermis at 250 nm than at 300 nm.
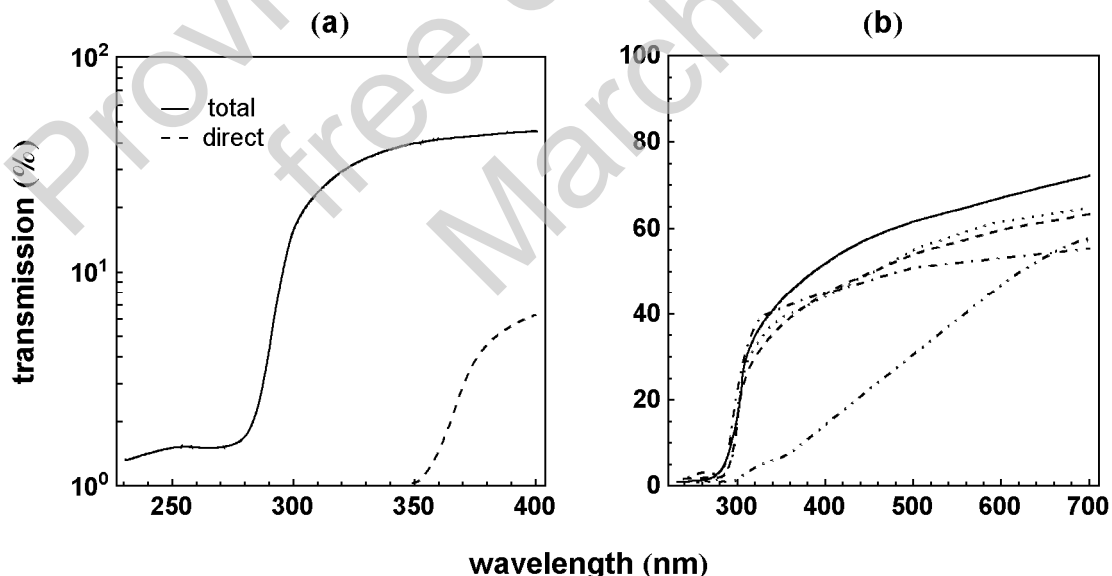

Figure 5. Spectral transmittance of human epidermis. (a) total and direct transmittance of one sample. (b) total transmittance of several samples. Adapted from Everett et al. [19].

The transmission of ultraviolet radiation through human stratum corneum and epidermis was later re-evaluated by Bruls et al. [21]. In their studies, the transmission of UV

5

radiation through the stratum corneum at 300 nm was approximately 30 %, while at 260 nm the transmission was approximately 8 %. The transmission of UV radiation through the epidermis showed the same dramatic decrease as reported by Everett [19], except the magnitude of the transmission was less than that reported by Everett in the UV-B and UV-C regions. They attributed this to exclusion of skin fluorescence and a different optical source. Figure 6 (adapted from Bruls et al. [21]) shows that the transmission of radiation at 260 nm is approximately only 1 % of the transmission at 300 nm.
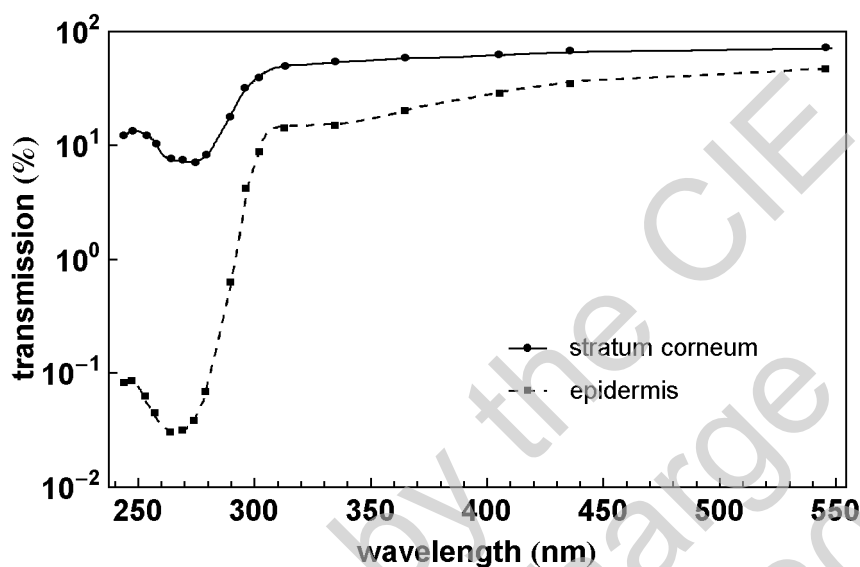

Figure 6. Average transmittance of stratum corneum and epidermis from non-exposed skin. Adapted from Bruls et al. [21].

Based on the observations of Bruls et al. [21], it would be expected that the carcinogenic potential of 250 nm – 260 nm radiation would be approximately 1 % of the potential at 300 nm; however, the target molecule for carcinogenesis, DNA, has an absorption maximum at 260 nm, with approximately 10-fold lower absorption at 300 nm [20]. In their calculation of a carcinogenesis action spectrum, DeGruijl and van der Leun [22] took into account the wavelength-dependence of carcinogenesis of ultraviolet radiation in mouse skin (SCUPm) and adjusted the values for the difference in transmission of ultraviolet radiation through mouse and human skin, arriving at the predicted carcinogenesis in human skin (SCUPh). The difference in carcinogenesis effectiveness between 260 nm and 300 nm radiation is approximately 100-fold [3, 22], and is consistent with the transmission of radiation through human skin shown in Figure 6.

3.5 Effect of Occupational UV-C Exposure on Non-Melanoma Skin Cancer (NMSC) Risk

Using the best available information, a lifetime exposure risk was calculated (see Appendix B) which showed that an accumulated daily exposure to 254 nm radiation at the ACGIH / ICNIRP threshold limit value (TLV) (i.e., 6 mJ·cm^{-2} (3 mJ·cm^{-2} effective), received over 8 h) for 5 days a week and over 20 years, would increase the risk of non-melanoma skin cancer by a factor of about 0,37 %. This calculation was based on a "worst case" exposure scenario, as a 2005 study by First et al. of 16 subjects in various facilities with upper room ultraviolet germicidal irradiation (UVGI) lamps indicated that even the highest of the measured 8 hour exposures were well below the TLV [23]. For example, the highest 8 hour exposure measured in that study was only 33,3 % of the TLV, the second-highest exposure was 20,8 % of the TLV, and 10 subjects received 8 hour exposures that were less than 5 % of the TLV. Indeed, a recent multi-centre field study of UV-C efficacy showed careful application of upper room UV-C lamps and lamp systems can be achieved without an apparent increase in the incidence of the most common side effects of accidental UV overexposure [24]. Further, the ACGIH UV hazard spectrum is based on the prevention of acute effects as well as chronic

6

effects on the eyes and skin; with respect to assessment of delayed effects, it is a much more conservative indicator for skin exposure risk to UV-C radiation than the more-realistic CIE action spectrum for photocarcinogenesis of non-melanoma skin cancers. The ACGIH UV hazard, CIE erythema, and CIE non-melanoma skin cancer (NMSC) action spectra are plotted in Figure 7 with the erythema and NMSC action spectra scaled down to reflect the UV hazard action spectrum's more conservative indication of chronic effects from UV-C radiation.
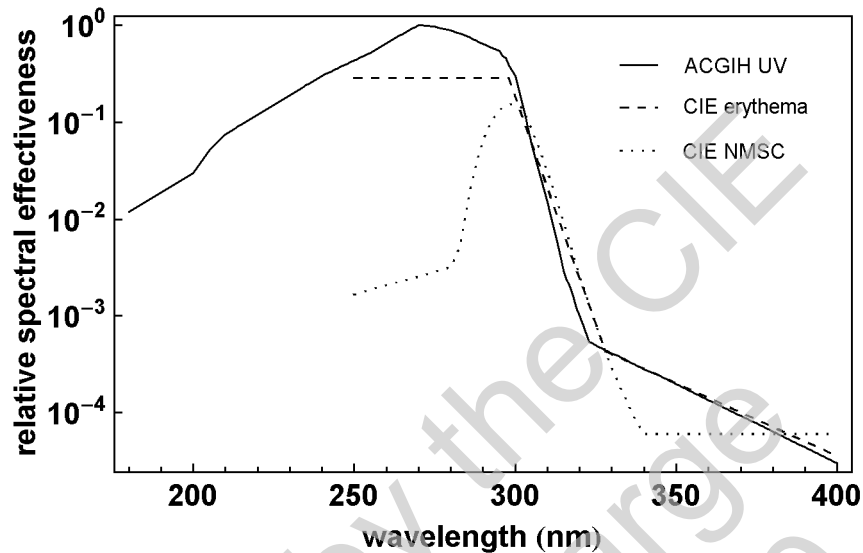

Figure 7. ACGIH UV hazard, CIE erythema, and CIE non-melanoma skin cancer (NMSC) action spectra are compared. The erythema and NMSC action spectra were reduced by a constant, for comparative purposes to demonstrate agreement at longer wavelengths. This figure demonstrates the decreasing of the action spectra values in the UV-C region because of the absorptance of the stratum corneum (erythema) and epidermis (NMSC). UV radiation must penetrate most of the epidermis to reach the germinative (basal) layer of the epidermis to pose a NMSC risk.

Hence, while the UV radiation from low-pressure mercury UVGI lamps has been identified as a potential carcinogen, the relative risk of skin cancer is significantly less than the risk from other sources to which a worker will be routinely exposed, such as solar radiation. UV germicidal irradiation can be safely and effectively used for upper-air disinfection without a significant risk of long-term delayed effects such as skin cancer.

4 CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH

Calculated estimates of NMSC risk show limited risk from the potential exposure from properly installed UV-C lamps and lamp systems where routine exposure remains below the applicable TLV.

If concerns about the potential risk of human skin carcinogenesis from UVGI remain, the recent developments of experimental techniques now permit a study of actual risk in humans. For example, a measurement of unrepaired DNA lesions induced by germicidal lamp (low-pressure mercury) radiation may be made in human skin using the p53 marker. This would indicate what exposure level would be of real concern and link the relative risk to that of UV-B radiation. Studies are also now possible for the photogenotoxicity of UV-C radiation to the skin and the skin responses to UV-C challenges (i.e., does UV-C induced apoptotic "sunburn" cells in human skin occur - perhaps only superficially - and does this evoke an appreciable expression of p53 and other stress signals?).

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ANNEX A A HISTORICAL NOTE

Potential Carcinogenic Effects for Human Skin of Ultraviolet Radiation of 253,7 nm Wavelength*

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* Unpublished presentation to the CDC 1999 Atlanta, GA

That ultraviolet radiation is able to kill bacteria has been known since the seminal observations of Downes and Blunt (1877).The most effective wavelength for this purpose is that produced by the mercury resonance line at 253,7 nm, since it is strongly absorbed by protein, particularly DNA.

For this reason, low-pressure mercury lamps have been used for many decades to disinfect a variety of materials, including room air. Since UVR can cause injury to skin and eyes, human exposure limits have been set by various technical organizations and regulatory agencies for occupational and public exposure. A limit of 6 mJ·cm^{-2} (i.e. 0,2 µW·cm^{-2} if continuous for an 8 hour day) has been set for 254 nm UV-C radiation (see "Threshold Limits for physical agents", issued by American Conference of Governmental Industrial Hygienists annually since 1969) (ACGIH, 2008). Earlier recommendations when UVGI was frequently used in hospitals were similar. For example, the Committee on Physical Medicine of the American Medical Association had recommended in 1948 a limit of 0,5 µW·cm^{-2} for continuous exposure to 7 hours per day to "germicidal ultraviolet radiation" (Illuminating Engineering Society (IES) Lighting Handbook 1987)

With the recent, disturbing increase in infection with M. Tuberculosis, room air disinfection has again become of great interest.

The minimal erythemal dose for untanned, fair human skin for UVR of wavelength 253,7 nm is on the average about 15 mJ·cm^{-2} to 25 mJ·cm^{-2} (CIE, 1998). The allowable daily exposure dose is 6 mJ·cm^{-2} per day, thus less than 0,5 MED.

The question has arisen whether chronic exposure of skin to such a dose could increase the incidence of skin cancer. There are several animal experimental studies on the carcinogenic effectiveness of germicidal ultraviolet radiation. Rush, Kline and Baumann (1941) were unable to produce skin cancers in mice with such radiation. Blum and Lippincott (1942) were able to produce a very small number of skin cancers, and concluded that most of the radiation was absorbed in the stratum corneum. They estimated that it took 40 times the UVR dose to induce skin tumors with germicidal radiation as compared to the effectiveness of the radiation from a medium-pressure mercury arc.

Forbes and Urbach (1974) were able to induce well-differentiated, non-metastasizing squamous cell carcinomas in hairless mice. In a 40-week treatment period, these animals received 7,5 J·cm^{-2}.

If one assumes the allowable irradiance of 0,1 µW·cm^{-2} for a 5 hour day, the daily dose will be 1,82 mJ·cm^{-2} or 657 mJ·cm^{-2} per year. The mouse dose (7,5 J·cm^{-2}) thus would be received in 11 years.

40 weeks is approximately half of a mouse lifetime. It is generally assumed that cancer development time is roughly related to the duration of life of the experimental animal, thus half a mouse lifetime can be conservatively equated to 30 years of human lifetime. Extrapolating the carcinogenic dose from mouse to man suggests that, given the ACGIH allowable exposure, a carcinogenic dose for human skin would require exposure for more than 300 years.

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NOTE: This document was circulated by Prof. Urbach to the original CIE TC 6-59 as the basis for its work.

ANNEX B   EFFECT OF OCCUPATIONAL UV-C EXPOSURE ON LIFETIME NON-MELANOMA SKIN CANCER RISK

One Attempt at Risk Quantification* -- A Sample Calculation Based Upon the Historical Note in Annex A

Assumptions and Caveats:

1. Assume a worst-case photocarcinogenesis-weighted daily exposure to UV-C radiation (254 nm) of 60 $J \cdot m^{-2} \cdot d^{-1}$, which is the exposure limit for 254 nm radiation recommended by the American Conference of Governmental Industrial Hygienists (1), and 5 work days per week:

   60 $J \cdot m^{-2} \cdot d^{-1}$ × 5 work days/week × 52 weeks/year × 0,011 383 (Relative photocarcinogenic effectiveness of 254 nm, reported in the ISO/CIE Standard for photocarcinogenesis of non-melanoma skin cancers (NMSC) [B1]) = 177,57 $J \cdot m^{-2} \cdot a^{-1}$ effective

   177,57 $J \cdot m^{-2} \cdot a^{-1}$ effective × 20 work years = 3,55 $kJ \cdot m^{-2}$ effective

2. Using Godar et al. [B2] data for annual erythemally weighted solar UV doses to general populations, not including vacation exposure: Northern Males 23 $kJ \cdot m^{-2}$, Southern Males 32 $kJ \cdot m^{-2}$, Northern Females 19 $kJ \cdot m^{-2}$, Southern Females 24 $kJ \cdot m^{-2}$. The annual UVR doses are based on solar UV measurements that were performed at various locations, and a percentage of these doses were then correlated to what would be received by a population. These data are used because no data are available for NMSC-weighted solar UVR doses to general populations. The annual doses were then assumed to apply over a lifetime of 70 years to give an estimated lifetime exposure.

3. Using the correlation from Scotto et al. [B3], increase in NMSC incidence for each 1 % increase in erythemally weighted UVR. BCC: Northern Males × 1,39, Southern Males × 2,10, Northern Females × 1,11, Southern Females × 1,68, SCC: Northern Males × 2,18, Southern Males × 3,31, Northern Females × 2,29, Southern Females × 3,4.

4. This sample calculation will also assume that the erythemally weighted solar UVR doses may be added with the worst-case estimates for NMSC-weighted exposures to 254 nm UV-C radiation. This appears to be reasonable in principle, because the 2003 CIE report on the spectral weighting of solar ultraviolet radiation [B4] indicated that the erythemally-weighted solar irradiances consistently correlated with the NMSC-weighted solar irradiances by a factor of 2,15 – 2,20 across a wide range of varying exposure conditions, such as varying solar zenith angles, total columns ozone, and altitude.

Lifetime erythemal exposure (70 years – age 5–75)		Additional exposure from UV-C, worst-case, 20 years	Increased BCC	Increased SCC
Northern Males	1 610 $kJ \cdot m^{-2}$	0,22 %	0,31 %	0,47 %
Southern Males	2 240 $kJ \cdot m^{-2}$	0,15 %	0,25 %	0,49 %
Northern Females	1 330 $kJ \cdot m^{-2}$	0,27 %	0,30 %	0,68 %
Southern Females	1 680 $kJ \cdot m^{-2}$	0,21 %	0,36 %	0,71 %
Possible average increase of NMSC:			0,31 %	0,59 %

5. Assuming incidence of 75 % BCC/25 % SCC, average NMSC increase 0,38 %
   Assuming incidence of 80 % BCC/20 % SCC, average NMSC increase 0,37 %

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* NOTE The reader is cautioned that any effort to quantify carcinogenic risk is subject to substantial uncertainties; however, for some this approach provides a reasonable estimate.

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ANNEX C   RECENT REFERENCES ON UV-C PHOTOCARCINOGENICITY

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    To investigate involvement of DNA mismatch repair in the response to short-wave ultraviolet (UV-C) light, we compared UV-C-induced mutant frequencies and mutational spectra at the Hprt gene between wild type and mismatch-repair-deficient mouse embryonic stem (ES) cells. Whereas mismatch repair gene status did not significantly affect survival of these cells after UV-C irradiation, UV-C induced substantially more mutations in ES cells that lack the MutSalpha mismatch-recognizing heterodimer than in wild type ES cells. The global UV-C-induced mutational spectra at Hprt and the distribution of most spectral mutational hotspots were found to be similar in mismatch-repair-deficient and wild type cells. However, at one predominant spectral hot spot for mutagenesis in wild type cells, the UV-C-induced mutation frequency was not affected by the mismatch repair status. Together these data reveal a major role of mismatch repair in controlling mutagenesis induced by UV-C light and may suggest the sequence context-dependent direct mismatch repair of misincorporations opposite UV-C-induced pyrimidine dimers.

2. MERRYMAN, J.I. Effects of ultraviolet C radiation on cellular proliferation in p53-/- keratinocytes. J Environ Pathol Toxicol Oncol, 18(1):1-9, 1999.

    Skin cancer is the most common tumor type in Caucasians, with an incidence that approaches the lifetime risk for all other cancer subtypes combined. The most common predisposing factor is exposure to ultraviolet (UV) radiation present in sunlight. The purpose of this investigation was to evaluate the effects of UV-C on the proliferation of a p53-/- human keratinocyte cell line, HaCaT, and how UV-C alters the response of these cells to transforming growth factors (TGF)-alpha and TGF-beta1. UV-C treatment during G0/G1 phase resulted in decreased incorporation of [3H]thymidine, an effect that was enhanced by pretreatment with TGF-beta1. However, irradiation of HaCaT cells in S or G2/M phase had no effect on the incorporation of [3H]thymidine, suggesting that these cells failed to undergo G2/M arrest in response to UV-mediated DNA damage. UV-C had no effect on TGF-beta1-mediated growth inhibition, but decreased the mitogenic response of HaCaT cells to TGF-alpha. Seven days after irradiation, there were no differences between the number of cells that were exposed to UV-C and those that were not, suggesting that the effects of UV-C on proliferation of HaCaT cells was transient. These results suggested that UV-C did not stimulate proliferation of p53-/- HaCaT cells, or cause cell cycle arrest in G2/M, which would allow transmission of chromosomal damage to daughter cells during M phase. Failure of the G2/M cell cycle checkpoint may be one of the mechanisms by which p53 results in genomic instability.

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    The CIE and ISO jointly published a Standard Action Spectrum for Non-Melanoma Skin Cancer (International Commission on Illumination, 2006; Photocarcinogenesis Action Spectrum (Non-Melanoma Skin Cancers); Standard ISO 28077:2006(E)/CIE S 019/E:2006). The standard is based on studies in laboratory animals and the resulting Skin Cancer Utrecht Philadelphia-man (SCUP-m) action spectrum (weighting function) modified to account for anatomical differences in human skin. Spectral and mathematical re-analyses confirmed that the SCUP-m weighting function accurately describes the tumor responses attributable to the ultraviolet radiation (UVR) sources used, and predicted that blocking the UVR scatter from the xenon long-arc solar simulator (i.e. minimizing the radiation < 290 nm) would have little or no measurable impact on tumor response in hairless mice. Data are now available from a direct laboratory test of that hypothesis. The methodology differed from previous studies only by virtue of modifying the lamp housing to

prevent the small but measurable amount of unfiltered, scattered radiation from reaching the mouse cages. Mice in two groups received weekly (Monday–Friday) UVR exposures totaling either 600 or 1200 Robertson-Berger Units, equivalent to 300 J·m^{-2} or 600 J·m^{-2} (CIE erythema-weighted), respectively. The median latent periods (for tumors > 1 mm planar diameter) were 37 and 23 weeks respectively. This response is well within the parameters of our published historical control data, all of which were based on the xenon lamp prior to its modification. This direct evidence lends further experimental support to the spectral specifications in the CIE/ISO Standard ISO 28077:2006(E)/CIE S 019/E:2006. The result further discounts recent speculation claiming that UVR scatter from the xenon UVR source substantially contributed to the observed tumor response, and thus skewed the calculated weighting function.