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SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS

SCCP

Opinion on

Biological effects of ultraviolet radiation relevant to health with particular reference to sunbeds for cosmetic purposes.

Adopted by the SCCP
during the 8th plenary of 20 June 2006

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1. Background

The main source of exposure to ultraviolet radiation (UVR) is the sun, but for some individuals substantial exposure occurs from artificial sources including sunbeds for cosmetic purposes, industrial lamps, arc welding and medical UVR therapies.

There is evidence that UVR can cause damage to health.

In the context of a notification under the safeguard procedure in accordance with Article 9 of the Low Voltage Directive (LVD) 73/23/EEC[1], a shortcoming in the European harmonised standard EN 60335-2-27:1997[2] has been brought to the attention of the European Commission by the Spanish authorities.

The LVD, a harmonisation Directive based on Article 95 of the EC Treaty, regulates the placing on the market of electrical appliances with a voltage rating between 50 and 1000 V (AC) and 75 and 1500 V (DC) with respect to health and safety. According to Article 95(3) of the EC Treaty[3] the LVD takes as its basis a high level of protection. Electrical appliances that comply with European harmonised standards under the LVD are presumed to comply with the corresponding essential health and safety requirements of the LVD.

The above mentioned shortcoming in the European harmonised standard EN 60335-2-27:1997, which has been reported to the European Commission, relates to the fact that the standard does not entirely cover the health and safety aspects which have to be considered during the design phase of the electrical appliance. In particular, it does not provide limit values on the maximum effective irradiance of UV radiation for the types of tanning devices that are covered by the scope of the standard.

In reaction to the notification and after consultation of governmental experts of Member States in the LVD ADCO[4] working group the Commission Services decided to request a scientific opinion from the "Non-Food Scientific Committees".

The scientific opinion will be used when preparing a Commission mandate to the European standardisation organisations regarding:

- the revision of the above mentioned standard EN 60335-2-27:1997;
- drafting or revising product related standards covering risks associated with the exposure of persons to ultraviolet radiation (UVR).

[1] Council Directive 73/23/EEC of 19 February 1973 relating to electrical equipment designed for use within certain voltage limits (OJ L 77, 26.3.1973); Directive as amended by Directive 93/68/EEC (OJ L 220, 30.8.1993)

[2] EN 60335-2-27:1997 "Safety of household and similar electrical appliances - Part 2-27: Particular requirements for appliances for skin exposure to ultraviolet and infrared radiation"

[3] Article 95 of the EC Treaty see: www.europa.eu.int/eur-lex/en/treaties/selected/livre221.html

[4] "Administrative co-operation" working group in the area of the LVD, consisting of the Market Surveillance representatives from all Member States and the European Commission

2. TERMS OF REFERENCE

The scientific committee is requested to answer the following questions in relation to the sunbeds for cosmetic purposes:

1. What are the general health and safety implications (negative and positive) relating to the exposure of persons to ultraviolet radiation (UVR)[5]?

2. What are the differences between risks associated with exposure of persons to natural UVR and those risks from artificial UVR? What are the differences regarding the health and safety risks with respect to exposure of persons to UVA, UVB and UVC radiation respectively?

3. Is the total dose value of UVR the only effective health and safety parameter with regard to the risks associated with exposure of persons to both natural and artificial UVR? What is the validity of the Bunsen-Roscoe law[6] over the range of irradiances and wavelengths associated with exposure of persons to both natural and artificial UVR?

4. What are the specific health and safety implications (negative and positive) relating to the exposure of persons to UVR from tanning devices for cosmetic purposes?

5. Are limit values necessary for the irradiance of UVR from artificial sources, in particular from tanning devices for cosmetic purposes, with respect to health and safety? Is it necessary to give different values for the irradiance of UV-A, UV-B and UV-C radiation respectively? If so, please specify the limit values for the irradiance of artificial UVR above which adverse health effects will occur. What are the uncertainties of these limit values?

6. Please specify the limit values of total dose of artificial UV-A, UV-B and UV-C radiation above which adverse health effects will occur, taking into account skin phototype, intensity of exposure, duration of exposure and associated uncertainties.

Supporting documents

- Spanish formal objection against European harmonised standard EN 60335-2-27
- ICNIRP statement (2003) (http://www.icnirp.org/documents/sunbed.pdf)
- WHO guidance brochure: artificial tanning sunbeds (2003) (http://www.who.int/uv/publications/en/sunbeds.pdf)
- ESA (European Sunlight Association) Position paper
- ESA (European Sunlight Association) frequently asked questions (http://www.europeansunlight.org/test/esa/html/faq.htm)
- NRPB: Health effects from Ultraviolet Radiation V13 No.1 2002 (http://www.nrpb.org/publications/documents_of_nrpb/pdfs/doc_13_1.pdf)
- NRPB: Advice on Protection Against Ultraviolet Radiation V13 No.3 2002 (http://www.nrpb.org/publications/documents_of_nrpb/pdfs/doc_13_3.pdf)

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[5] The International Commission on Illumination (CIE) defines ultraviolet radiation (UVR) as optical radiation between 100 and 400 nm. The spectral region is divided into three photo-biological spectral regions: UVC (l00-280 nm), UVB (280-315 nm) and UVA (315-400 nm).

[6] The Bunsen-Roscoe law (law of reciprocity) states that a certain biological effect is directly proportional to the total energy dose irrespective of the administered regime. Dose is the product of intensity and the duration of exposure. (Bunsen R, Roscoe HE, Photochemische Untersuchungen, Poggendorff˝s Annalen 1855: 96: 373-394, 1857: 100: 43-88 and 481-516, 1857: 101:235-263, 1859: 108: 193-273.).

- SSK: Schutz des Menschen vor den Gefahren der UV-Strahlung in Solarien (http://www.ssk.de/2001/ssk0101w.pdf)
- Scientific investigations from ECO**FYS**
- Other documents

National and international organisations contributing to the discussion

- ICNIRP - International Commission on Non-Ionizing Radiation Protection (http://www.icnirp.org)
- WHO - World Health Organization (http://www.who.int)
- IARC - International Agency for Research on Cancer (http://www.iarc.fr)
- UNEP - United Nations Environment Programme (http://www.unep.org/PDF/Solar_Index_Guide.pdf)
- NRPB - National Radiological Protection Board (UK) (http://www.nrpb.org)
- SSK – Strahlenschutzkommission (Germany) (http://www.ssk.de)
- IMM – Institute of Environmental Medicine (Sweden) (http://www.imm.ki.se)
- EPA - U.S. Environmental Protection Agency (US) (http://www.epa.gov)
- FDA - U. S. Food and Drug Administration (US) (http://www.fda.gov)
- NIES - National Institute for Environmental Studies (JP) (www@nies.go.jp)
- List of experts provided by ESA (European Sunlight Association)

3. OPINION

The cosmetic purpose of using a sunbed is to achieve a tan. The tanning effect has been demonstrated and quantified in a study that followed a Food and Drug Administration (FDA) protocol (Caswell, 2000) with 3 weekly exposures for 8 weeks. A significant tanning effect was evident after 6 exposures and the level of tan increased steadily over the 8-week assessment period. Another study, with twice weekly exposure for 6 weeks, demonstrated tanning (Ruegemer et al, 2002).

Commercial sunbeds were developed in the 1970s and came into widespread use in the 1990s. Thus, the full health effects of artificial tanning are not yet known. It will take several years before the real picture of the role of the sunbeds in inducing skin cancer becomes fully apparent, due to the long induction period of this disease.

In this Opinion, the term "sunbed" refers to all types of UV tanning devices for cosmetic purposes.

The six questions raised in the Terms of Reference have also been addressed by van der Leun and Forbes (2005).

1. What are the general health and safety implications (negative and positive) relating to the exposure of persons to ultraviolet radiation (UVR)?

1.1 Negative Effects

1.1.1 Acute

Skin

Exposure of the skin to solar UVR (~ 295 – 400 nm) results in inflammation (erythema/sunburn) that is usually maximal about 24 hours later (Farr et al, 1988). This response is primarily induced by its UVB component (~295-315nm) (see section 2(b).1) and is associated with increased blood flow (Young et al, 1985), increased sensitivity to thermal and mechanical stimuli (Harrison et al, 2004), a dermal inflammatory infiltrate (Gilchrest et al, 1983; Hawk et al, 1988) and the presence of apoptotic keratinocytes know as sunburn cells (Sheehan and Young, 2002). Individual sensitivity to erythema can be assessed by determining the minimal erythema dose (MED) that increases with skin type as shown in Table 1 but MED is not predictive of skin type because there is considerable variation of MED within different white skin types (Harrison and Young, 2002). Within a few days of exposure to solar UVR delayed melanogenesis (tanning) occurs that is dependent on skin type and like erythema is primarily caused by UVB. This results from the synthesis of melanin in melanocytes: specialized pigment producing cells in the epidermis that transfer melanin to keratinocytes. Many people expose themselves to UVR, either from the sun or sunbeds, for the sole purpose of obtaining a tan that becomes more intense with repeated exposure. This repeated exposure also results in thickening of the epidermis, especially the *stratum corneum*, the outermost dead layer, which results in the skin feeling dry. The UVA content of solar UVR makes a relatively small contribution to erythema and tanning (see section 2(b).1). A UVB tan is photoprotective against erythema but the level of photoprotection is modest and equivalent to a sunscreen with a sun protection factor (SPF) of 2-3 (Agar and Young, 2005). However, tans primarily induced by UVA are not photoprotective against erythema

(Gange et al, 1985). UVR exposure, in particular UVA, results in transient immediate pigment darkening (IPD) the function of which is not known (Routaboul et al, 1999).

Table 1: A classification of skin phototypes based on susceptibility to sunburn in sunlight, together with indicative MEDs that might be expected following UV exposure on unacclimatized skin

Skin Photo Type	Sunburn Susceptibility	Tanning Ability	Classes Of Individuals	No. in SED[§] for 1 minimal erythema dose (MED)
I II	High High	None Poor	Melano-compromised	1 - 3
III IV	Moderate Low	Medium Dark	Melano-competent	3 - 7
V VI	Very low Extremely low	Natural brown skin Natural black skin	Melano-protected	7 - >12

[§] The unit of erythemal radiation is the Standard Erythema Dose (SED), where 1 SED is equivalent to an erythemal effective radiant exposure of 100 Jm^{-2} (CIE 1998). It requires an exposure of about 3 SED to produce just minimal erythema in the unacclimatized white skin of the most common northern European skin types (Harrison & Young 2002). An exposure of 5-8 SED will result in moderate sunburn and 10 SED or more can result in a painful, blistering sunburn.

Solar UVR exposure can aggravate certain skin diseases such as lupus erythematosus and pemphigus (Morison et al, 1999) and induce skin photosensitivity with commonly used UVR-absorbing systemic drugs and topically encountered chemicals (Ferguson et al, 1999). Furthermore, there is a wide range of acquired and genetic UVR and visible radiation photodermatoses that are beyond the scope of this document.

Exposure of the skin to UVR can suppress cell-mediated immunity when assessed with the sensitisation (Kelly et al, 2000) and the elicitation arms (Moyal and Fourtanier, 2003) of the contact hypersensitivity (CHS) response. A single sub-erythemal exposure of solar simulating radiation (SSR) suppresses the induction (sensitisation) arm of the CHS response in skin types I/II (Kelly et al, 2000) but erythemal exposure is necessary to suppress the elicitation arm (Moyal and Fourtanier, 2003). Suppression of cell-mediated immunity is thought to play a role in UVR-induced skin cancer and infectious diseases, e.g. Herpes simplex infections.

The clinical effects of UVR exposure, whether acute or long-term, are underpinned by many molecular and cellular events (Matsumura and Ananthaswamy, 2002). UVR-induced damage to epidermal DNA, especially cyclobutane pyrimidine dimers (CPD), is thought to be responsible for many adverse effects of solar UVR, including immunosuppression, and can be demonstrated in the skin immediately after exposure to erythemal and sub-erythemal UVR (Young et al, 1998). DNA integrity is maintained by complex repair processes and the p53 mediated elimination of damaged cells by apoptosis (sunburn cell formation). Failure of these processes is though to result in skin cancer (Matsumura and Ananthaswamy, 2002). Membrane as well as DNA effects also contribute to UVR-induced skin damage. The relevant cell surface or cytoplasmic chromophores are currently unknown. There is considerable evidence that the photoisomerization of stratum corneum trans-urocanic acid (UCA) to the cis-form also plays an important role in immunosuppression. Exposure to erythemal UVR or repeated sub-erythemal UVR results in a loss of epidermal antigen presenting Langerhans cells (Novakovic et al, 2001).

Eye

The eye is a complex multi-layered organ that receives visible radiation on its retina. The intermediate layers attenuate UVR to different degrees and thereby protect the retina from UV photodamage. The outermost cornea absorbs UVC and a substantial amount of UVB, which is further attenuated by the lens and the vitreous humor in front of the retina. UVA is less well attenuated by the cornea but is attenuated by the internal structures so it does not reach the retina (Sliney, 2001; Roberts, 2001; Johnson, 2004).

The only acute clinical effect of UVR on the eye is photokeratitis that is also known as snow blindness or welder's flash (Sliney, 2001; Roberts, 2001; Johnson, 2004). This is a painful transient inflammatory condition caused by UVC and UVB-induced damage to the corneal epithelium. Typically it appears 6-12 hours after exposure and resolves, within 48 hours. In some ways it can be regarded as sunburn of the eye.

1.1.2 Chronic

Skin Cancer

An IARC monograph on solar and ultraviolet radiation classified solar radiation as "carcinogenic" to humans (Group 1) and UVA and UVB and the use of sunbeds as "probably carcinogenic" to humans (Group 2A)(IARC, 1992).

Non-melanoma

Solar exposure is recognized as the main environmental factor in the development of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) that form the great majority of skin cancers (IARC, 1992). These lesions result in a high level of morbidity with only occasional mortality from infrequent metastatic SCC. UVR is also associated with actinic keratoses (AK) that may be regarded as precancerous lesions for SCC.

The evidence for UVR in these lesions has been primarily ecologic (reviewed by Armstrong and Kricker, 2001), supported by mouse studies in the case of SCC (de Gruijl, 1995). More recently, a role for UVR has been supported by the presence of UVR "signature mutations" in tumours (Brash et al, 1996). Skin type is an important determinant of BCC and SCC risk with skin types I and II at greater risk than skin types III and IV, with the lowest risk being in skin types V and VI. SCC is associated with chronic UVR exposure and is more common in people with outdoor occupations. There is evidence that BCC is associated with intermittent exposure (Kricker et al, 1995). Many cancer registers do not record BCC and SCC. Melanoma has been registered for many years and there is evidence that the incidence rate is increasing substantially in Europe (Boyle et al, 2004). Data from the skin cancer registry in Trentino, Italy showed incidence rates of 88 per 100,000 for BCC and 29 per 100,000 for SCC in the period 1993-1998 in comparison to 14 per 100,000 for melanoma (Boi et al, 2003).

Melanoma

Though much less common than BCC and SCC, melanoma is the main cause of death from skin cancer. There were an estimated 35,000 cases of melanoma diagnosed in Europe in 2000 with 9000 deaths (Boyle et al, 2004). Sun exposure is established as the major environmental determinant of melanoma (IARC, 1992; Donawho et al, 1994; Armstrong and Kricker, 1993) and the risk of melanoma depends on the interaction between environmental exposures and the genes which determine susceptibility. Melanoma is rare in black skinned peoples (Parkin et al, 1997).

There is no doubt that skin colour and sun exposure are potent determinants of risk of melanoma. World incidence figures show that the risk to individuals is greatest where pale skinned peoples live at low latitudes such as Australia and New Zealand (Parkin et al, 1997; Bulliard, 2000). In areas of the world where dark and pale skinned peoples live at high UV exposure levels, such as Hawaii, then the risk to pale skinned people is much greater than for their darker skinned neighbours (Chuang et al, 1999). Within Europe there is variation in incidence which reflects the interaction between skin colour and latitude as the peak incidence is in the north, in countries such as Sweden, where fair skinned peoples live an outdoor life and have access to sunny holidays in the south, or Switzerland where fair skinned peoples live at high altitude (Parkin et al, 1997). So, in the period 1996-8 the incidence rates (European Standardised Rates) in women were reported to be 17 per 100,000 in Switzerland, 6 per 100,000 in Spain and 16 per 100,000 in Sweden (de Vries and Coebergh, 2004).

Broadly, it would be reasonable to conclude that the risks of melanoma are so low in black-skinned peoples that sun protection advice should be directed only towards white-skinned peoples. The difficulty here is that skin colour is a continuous rather than a discontinuous variable. Some Asian peoples have quite a high tendency to burn and within white skinned peoples there is variation in susceptibility to sunburn and to melanoma which is related to skin colour and whether there are freckles or not. Data from many case control studies have established that phenotypic characteristics associated with vulnerability to the sun are risk factors for melanoma. Gandini et al (2005a) recently summarized these in a meta-analysis of 60 such studies. Her overall conclusions were that skin type I (versus IV) was associated with a relative risk (RR) of 2.1 for melanoma (95% CI 1.7-2.6), where skin type I, is skin which always burns and never tans and skin type IV is skin which never burns. A high density of freckles was associated with a RR=2.1 (95% CI 1.8-2.5), eye colour (Blue vs. Dark: RR=1.5, 1.3-1.7) and hair colour (Red vs. Dark: RR=3.6, 2.6-5.4). Hence, whatever the ethnic origin of Europeans, in terms of skin type, health advice about skin cancer should be directed to those individuals with a tendency to burn rather than to tan, those who have freckles and those with fair (particularly red) hair. It is clear from the level of these risk factors that the relative risk is significant but the absolute risk associated with these phenotypic characteristics is relatively small in European countries with incidence rates of between 5 and 17 per 100,000 per annum (European Standardised Rates) (de Vries and Coebergh, 2004). The prevalence of individuals with these risk factors will vary considerably between populations. In a study of healthy women in the UK, 8% had red hair and 6% had very high freckle scores on the back (Bertram et al, 2002).

Risk of melanoma is also greater in patients with larger numbers of melanocytic naevi whether banal or clinically atypical, where an atypical naevus is defined as a mole 5mm or greater in diameter, with an irregular or ill-defined edge and variable pigmentation. Numerous case-control studies have addressed this, and a second meta-analysis by Gandini et al (2005b) showed that the number of common naevi was confirmed as an important risk factor for melanoma with a substantially increased risk associated with the presence of 101-120 naevi compared with <15 (pooled Relative Risk (RR) = 6.9; 95% Confidential Interval (CI): 4.6, 10.3) as was the number of atypical naevi (RR = 6.4 95%; CI: 3.8, 10.3; for 5 versus 0). Twin studies have provided strong evidence that naevus number is genetically determined (Wachsmuth et al, 2001; Zhu et al, 1999; Easton et al, 1991) and the association of the phenotype with melanoma risk therefore implies the presence of naevus genes, which are also low penetrance melanoma susceptibility genes. Thus, persons with this atypical naevus phenotype have an increased risk of melanoma, which is significantly higher than that associated with red hair or freckles. The prevalence of this phenotype also varies between populations but was reported in 2% of individuals in the UK (Bataille et al, 1996).

The phenotypes described above are genetically determined and therefore it is not surprising that family history is a risk factor for melanoma. Familial melanoma was reported in the 19th century in the UK (Norris, 1820), and a strong family history of melanoma is the most potent risk factor for melanoma (Kefford et al, 1999). Any family history of melanoma is associated with a doubling of risk for close relatives. A study from the Utah population database estimates risk to first-degree relatives of melanoma cases to be 2.1 (95% CI 1.4-2.9). A similar study from the Swedish Cancer Registry estimated the standardized incidence ratio for melanoma to be 2.4 (95% CI 2.1-2.7) for offspring if one parent had a melanoma, 3.0 (95% CI 2.5-3.5) for an affected sibling and 8.9 (95% CI 4.3-15.3) if a parent and a sibling were both affected. The highest ratio was 61.8 (95% CI 5.8-227.2) for offspring when a parent had multiple melanomas (Hemminki et al, 2003). Such patterns of risk are indicative of a significant hereditary component, which is most probably inherited as an autosomal dominant trait with incomplete penetrance. The risk of melanoma increases with age although in Europe the age distribution curve is relatively flat and in Europe the incidence is commonly higher in women than in men (Parkin et al, 1997).

Sun exposure is clearly the major environmental risk factor for melanoma as discussed above. A third meta-analysis reported by Gandini et al (2005c) has supported the conclusions of many individual case-control studies that intermittent sun exposure remains the most predictive environmental risk factor for melanoma (random effects model RR=1.6 (95% CI 1.3-2.0) and that sunburn, especially in childhood is a significant risk factor, although there was much heterogeneity between studies. A random effects model suggested a highly significant effect for sunburn at any age (RR=2.0 95% CI 1.7-2.4). The pooled analysis provided no evidence for a causal effect of chronic sun exposure on melanoma risk, RR=1.0 (95% CI 0.9-1.0). Further evidence for a role of sun exposure in melanoma comes from penetrance studies for the melanoma susceptibility gene CDKN2A in which there was evidence for an interaction between susceptibility genes and latitude of residence so that penetrance was highest in families with germline CDKN2A mutations living in Australia when compared with those in Europe (Bishop et al, 2002).

A meta-analysis, incorporating latitude, showed that phenotypic indicators of excessive sun exposure (representing gene/environment interaction) in fair-skinned individuals are risk factors for melanoma (Gandini et al, 2005a). Pre-malignant and malignant lesions were associated with a RR=4.3 (2.8-6.6) and actinic damage indicators with a RR=2.0 (1.2-3.3). This is of note despite the lack of epidemiological evidence from case-control studies for chronic sun exposure as a risk factor for melanoma.

In summary, there is strong evidence that excessive sun exposure is causal for melanoma. Evidence persists that the exposure pattern is important, e.g. intermittent, although the observation in some studies that actinic skin damage is a risk factor provides some evidence that chronic over-exposure is also causal in some patients. The evidence is also strong that excessive sun exposure increases the risk of melanoma in those with a strong family history. There is an emerging view, based upon epidemiological and biological studies that there may be more than one route to melanoma: one associated with low or intermittent sun exposure and for which numerous naevi is a risk factor and another with chronic over exposure (Whiteman et al, 2003). All of the risk factors quoted above are independent risk factors in individual case control studies and therefore the presence of multiple risk factors in an individual increases the relative risk of melanoma.

Health education is postulated to be most effective when targeted at those at greatest risk. Thus, UVR risk communication to European citizens is probably best directed at those with established risk factors (e.g. family history, fair skin and multiple naevi). There is a need to communicate these complex issues to the European citizen in a way that is easily understood.

Photoageing

Exposure of the skin to UVR results in UVR-induced skin ageing known as photoageing, which is very evident, when one compares normally sun-exposed (face) and sun-protected (buttock) sites. Clinical symptoms of photoageing include wrinkling, laxity and disturbances of the distribution of pigmentation (Glogau, 1996). Photoageing is thought to at least partially arise from the induction of matrix metalloproteinases (MMPs) that degrade collagen, the major structural protein of the dermis (Fisher et al, 2002). Photoageing, assessed by elastosis, is an indicator of non-melanoma skin cancer risk (Kricker et al, 1991).

Effects on the Eye

There is epidemiological evidence that solar UVR exposure increases the risk of cataracts of the lens, anterior lens capsular change and pterygium (Johnson, 2004). *In vivo* and *ex vivo* acute studies on mammalian lens (Pitts et al, 1977; Merriam et al, 2000; Oriowo et al, 2001) and a chronic *in vivo* study (Jose and Pitts, 1985) have indicated that the UVB part of the solar spectrum is most likely to be responsible for any long term effects that solar UVR has on the lens. There is also epidemiological evidence that solar UVR exposure results in ocular melanoma, especially from a study in Australia (Vajdic et al, 2002) that showed that choroid and ciliary body melanoma were positively associated with time outdoors on weekdays with OR up to 1.8 (95% CI 1.1 – 2.8) and p = 0.01 for trend. Unlike melanoma of the skin there is no latitude gradient for ocular melanoma (Vajdic et al, 2003), which may be because UVR dose to the eye is probably determined by UVR exposure from horizon sky that is less affected by latitude.

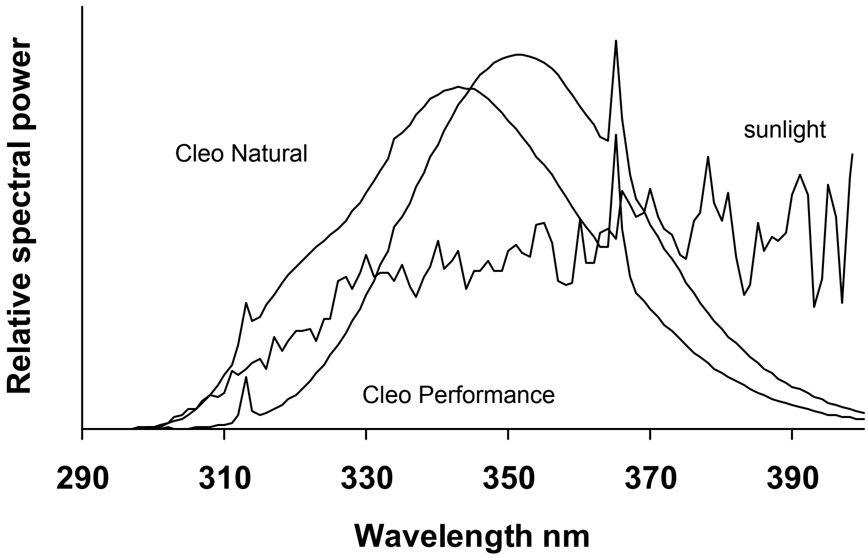
1.2 Positive Effects

Exposure to solar UVB initiates the synthesis of vitamin D, in the skin, that is vital for musculo-skeletal health (Vieth, 2005) and there is evidence that large numbers of people are vitamin D insufficient (Holick, 2005). Rickets, widespread in industrialized cities in 19th century Europe, is being increasingly diagnosed in ethnic minority populations in Northern and Southern Europe and can be attributed to vitamin D deficiency (Pedersen, 2003; Yeste and Carrascossa, 2003; Ladhani et al, 2004; Mallet et al, 2004). There is also emerging evidence, as yet mainly ecologic (i.e. by association), that vitamin D is important in other aspects of health such the prevention of autoimmune disorders (Ponsonby et al, 2005) and several internal malignancies (Berwick and Kesler, 2005; Giovannucci et al., 2006). There are also recent data suggesting that vitamin D may be important in improving outcome from cancer (Chen and Holick, 2003; Zhou et al, 2005). Exposure to the sun may therefore have widespread beneficial effects but it seems likely that these beneficial effects would also be produced by increased oral intake of vitamin D. However, the role of vitamin D in non-skeletal health, along with its association with UVR exposure remains a very controversial area and more data are needed for informed discussion.

2(a) What are the differences between risks associated with exposure of persons to natural UVR and those risks from artificial UVR?

There are no physical differences in type of radiation between natural and artificial UVR *per se*. However, there are important differences in the spectral distribution and absolute and relative irradiances of UVR from the sun and artificial sources, and between different artificial sources as shown in Figure 1. There is no standard solar spectrum because this varies with factors such as season, latitude and time of day. From a physical standpoint, the UV emission from sun is primarily within the UVA range. Artificial emission spectra are different from solar emission spectra from a physical point of view.

It is relatively easy to compare the acute risks of exposure to natural and artificial UVR, which are similar, the details of which are discussed in Section 4. It is much more difficult to compare chronic effects which, in the sun, also depend on patterns of exposure.



¶ Measured in Melbourne (38° S) at solar noon on 17 January 1990. Measurements were made at the Australian Radiation Laboratory with a Spex 1680B double monochromator with a resolution of 1 nm

Figure 1 Emission spectra of solar UVR and two tanning lamps (i) Cleo natural and (ii) Cleo performance

Data on the risk of skin cancer associated with artificial UVR sources (see Section 4) are few compared with those related to sun exposure. Furthermore the tanning device studies are often uninformative because of small numbers of cases and controls, and low usage of the devices. There are also great difficulties in collecting adequate exposure data because of recall bias and lack of user knowledge of the type of UVR emitted by the devices. Many studies therefore have recorded only whether a tanning device has been used "ever" or "never" so that the power to address dose or age effects is limited.

Furthermore, tanning device users are often those who sunbathe frequently and it is likely that case-control studies are seriously confounded. There are some data published on the effects of medical use of artificial UVR sources. Although the UVR dose is considerably lower than that to which users of tanning devices are potentially exposed, such studies do have the merit of much more accurate dosage estimation.

Photo(chemo)therapy is used in the treatment of skin diseases. The use of psoralen plus UVA (PUVA) to treat psoriasis is known to cause skin cancer (Stern and Laird, 1994) but PUVA is mechanistically quite different from UVA and UVB and therefore is not relevant to the current discussion. In the PUVA cohort study reported by Stern from the United States, there was no discernable additional effect of exposure to UVB (Stern and Laird, 1994). In a study of psoriatics treated with coal tar and UVB in the 1950s followed up for 25 years there was no demonstrable increased risk of skin cancer but the numbers treated were relatively small (280) (Pittelkow et al, 1981). In an even smaller study of 195 German psoriatics treated with broadband (n=69) or narrow band UVB (n= 126) from 1994 to 2000 only one skin cancer had occurred by 2004. This was an *in situ* melanoma which developed in the same year that narrow band UVB therapy was begun (Weischer et al, 2004). A study in Scotland with a median follow up period of 4 years has shown a small increase in BCC after treatment with narrow band UVB phototherapy (Man et al, 2005).

Overall, the risks of skin cancer from the medicinal use of artificial UVR (in the absence of photosensitizers) appear to be small but the data are few and the dose to which the patients are exposed tends to be significantly smaller than users of commercial sunbeds are potentially exposed to. It is likely, from our knowledge of skin cancer and solar UVR, that the skin cancer risk attributable to artificial UVR will be greater in those who are genetically susceptible such as the fair skinned.

Household lights emit significant amounts of UVR (Sayre et al, 2004) and several case-control studies have addressed risk for melanoma associated with such exposure. The earliest study suggested an elevated risk associated with exposure to fluorescent lights at work (Beral et al, 1982) but all subsequent studies failed to identify such a risk (Osterlind et al, 1988; Rigel et al, 1983; Walter et al, 1992; Holly et al, 1995).

2(b) What are the differences regarding the health and safety risks with respect to exposure of persons to UVA, UVB and UVC radiation respectively?

Coblentz introduced the concept of the spectral regions UVA, UVB and UVC at the Second International Congress on Light in Copenhagen in 1932. These regions were determined by the transmission properties of three common glass filters; a barium-flint filter defined the UVA (315-400nm); a barium-flint-pyrex filter the UVB (280-315nm); and a pyrex filter defined the

UVC (wavelengths shorter than 280nm). So the basis of these divisions has its grounding in physics, and not biology, although these definitions have been very useful in biology. Although these are the official designations of the Commission Internationale de l'Éclairage (CIE), other authorities, especially in the biological and clinical sciences, use different definitions such as UVA (320-400nm), UVB (290-320nm) and UVC (190-280nm). More recently, the terms UVA-I (340-400nm) and UVA-II (315-340nm) have come into use because of a better understanding of mechanistic differences between UVB and UVA. Mechanistically, UVA-II is similar to UVB in which the target molecule (e.g. DNA) is directly altered by its absorption of UVR energy. In contrast, UVA-I reactions tend to cause indirect damage to target molecules via reactive oxygen species (ROS) generated by UVR absorption by other molecules.

2(b).1 Acute Effects

The wavelength dependency of a given photobiological effect is demonstrated by its action spectrum, which depends on a variety of factors but is based on the absorption spectrum of the chromophore (UVR absorbing biomolecule) and the optical properties of the skin. Action spectroscopy and studies with different broad-spectrum sources show that UVB is much more effective than UVA for most acute endpoints studied in human skin. This includes erythema (Anders et al, 1995; CIE 1998; Young et al, 1998), delayed pigmentation (Parrish et al, 1982), DNA photodamage (Young et al, 1998) and UCA photoisomerization (McLoone et al, 2005). In general, UVB is 3 to 4 orders of magnitude more effective per unit physical dose (J/cm^2) than UVA, but this difference depends on the specific wavelengths/wavebands being compared. Action spectra for immunosuppression in human skin are not available. UVB is known to be immunosuppressive but the role of UVA is still not clear (Phan et al, 2006). The action spectrum for IPD shows that UVA is more effective than UVB (Irwin et al, 1993).

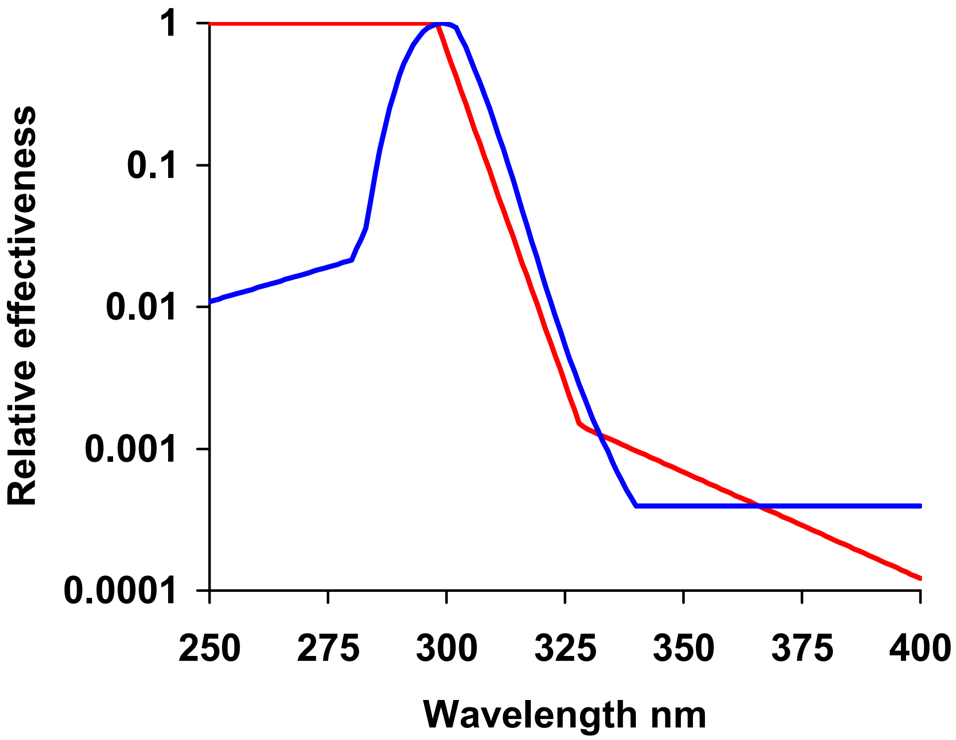
UVC is not an issue for terrestrial solar UVR because it is completely absorbed by the ozone layer. In any case, UVC is strongly attenuated by chromophores in the upper epidermis (Young, 1997) and UVC-induced DNA damage in the dividing basal layer of human epidermis is not readily detected (Campbell et al, 1993; Chadwick et al, 1995) which may explain why the dose response curve for UVC erythema in human skin is very much less steep than for UVB (Diffey and Farr, 1991). It is unlikely that UVC from artificial sources presents an acute or long-term hazard to human skin. However, UVC is likely to cause acute photokeratitis.

Wavelength dependency is crucial in determining the biological effect of a given spectral region of a UVR source. For example, the 0.8% UVB content of a tanning lamp accounted for 75% of the CPD (cyclobutane pyrimidine dimers) that it induced in human keratinocytes *in vitro* (Woollons et al, 1999). Thus action spectra are essential as weighting functions to determine the biological effects of different broad-spectrum UVR emission spectra (see Section 5). Emission spectra without relevant action spectrum weighting are of very limited value in risk assessment. Action spectra are only valid if there is no interaction between different spectral regions. However, there is evidence that such interactions do occur at the cellular level (Schieke et al, 2005).

2(b).2 Chronic Effects

The wavelength dependencies for skin cancer (SCC) and photoageing (elastosis) have been determined in hairless mouse models (de Gruijl, 1995; Kligman and Sayre, 1991) and these studies have shown action spectra similar to that for human erythema (CIE, 1998; Young et al, 1998). Figure 2 shows the action spectra for human erythema and non-melanoma skin cancer (SCC) (CIE 1998, 2000) and it can be seen that these are very similar, especially in the solar UVB and UVA-II (315-340nm) ranges. Thus, one might conclude that erythema, primarily caused by UVB, can be regarded as a surrogate risk factor for SCC and photoageing. There is no animal model for UVR-induced BCC.

Figure 2: The CIE (1987) reference action spectrum for erythema in human skin (red) and the estimated CIE (2000) action spectrum for human squamous cell carcinoma (blue) based on mouse studies



Sunburn, an important risk factor for melanoma, has therefore implicated UVB in its pathogenesis (Wang et al, 2001). The incidence of melanoma, as well as BCC and SCC, is very high in xeroderma pigmentosum (XP) with defective excision repair of UVB-type DNA damage, e.g CPD. The wavelength dependency for melanoma however is not yet established because of the lack of a good animal model (Noonan et al, 2003). Melanomas have proved extremely difficult to induce by UVR alone in mice. Wavelength dependency has been determined in a fish model (*Xiphophorus*) (Schartl et al, 1997) the value of which is limited because its melanoma-like lesions arise from the dermis instead of the epidermis and fish are phylogenetically very different from humans. Studies in these fish however showed that visible and UVA radiation, as well as UVB (Setlow et al, 1993) induced lesions that raised concern that UVA might be causal for human melanoma as well or instead of UVB. A mammalian opossum model also developed melanoma-like lesions after broad-band UVA exposure but with low potency compared to broad-band UVB (Robinson et al, 2000). A mouse model was described in 2003 (the hepatocyte growth factors/scatter factor transgenic mouse) in which melanomas with a strong epidermal component were induced (Nonnan et al, 2003). Neonatal UV irradiation was necessary and sufficient to induce melanoma although adult irradiation increased the number of lesions. In 2004 the same group reported studies using the mouse in which UVB but not UVA induced melanoma, providing perhaps more persuasive evidence that UVB exposure is causal rather than UVA (De Fabo et al, 2004).

Studies of somatic mutations in a variety of genes have been reported in the search for evidence to support a role for UVB exposure. Genes such as p53 have, however, failed to show the characteristic UVB signature C to T transitions and CC to TT mutations, providing additional concern that UVB may not be the only causal waveband. Recently, mutations in BRAF (downstream of RAS) were found in a majority of naevi and melanoma. The dominant point mutation (T1796A) is not characteristic of UVB radiation, but this does not exclude a causal role for UVR (de Gruijl, 2003).

It is more difficult to determine UVA induced mutagenesis because DNA does not significantly absorb UVA at doses obtained with solar exposure. It is thought that UVA induced mutagenesis is mainly mediated by photosensitising reactions that generate reactive oxygen species. In one system it was suggested that T to G transversions are typical of UVA induced damage (Drobetsky et al, 1995) but in another G to T transversions were seen as well as small tandem base deletions (Pfeifer et al, 2005). There is no consensus on UVA signature somatic mutations in tumours. Furthermore, it is possible that UVA may have an indirect adverse effect on the micro-environment in the dermis and dermo-epidermal junction by inducing growth factor release which may have a proliferative effect on melanocytes (Brenner et al, 2005).

In summary, UVB is likely to be the main cause of photoageing and SCC. Sunburn, a marker for excessive UVR exposure, is a risk factor for melanoma. UVB is the main cause of sunburn but this does not necessarily mean that it is the prime cause of melanoma, the spectral dependence of which remains unknown. The conservative approach is to restrict UVB and UVA exposure in susceptible phenotypes until wavelength dependency is established. UVC exposure is unlikely to cause acute or long-term damage to the skin but can cause severe acute damage to the eye and should not be permitted at all from any tanning device.

3 (a) Is the total dose value of UVR the only effective health and safety parameter with regard to the risks associated with exposure of persons to both natural and artificial UVR? (b) What is the validity of the Bunsen-Roscoe law over the range of irradiances and wavelengths associated with exposure of persons to both natural and artificial UVR?

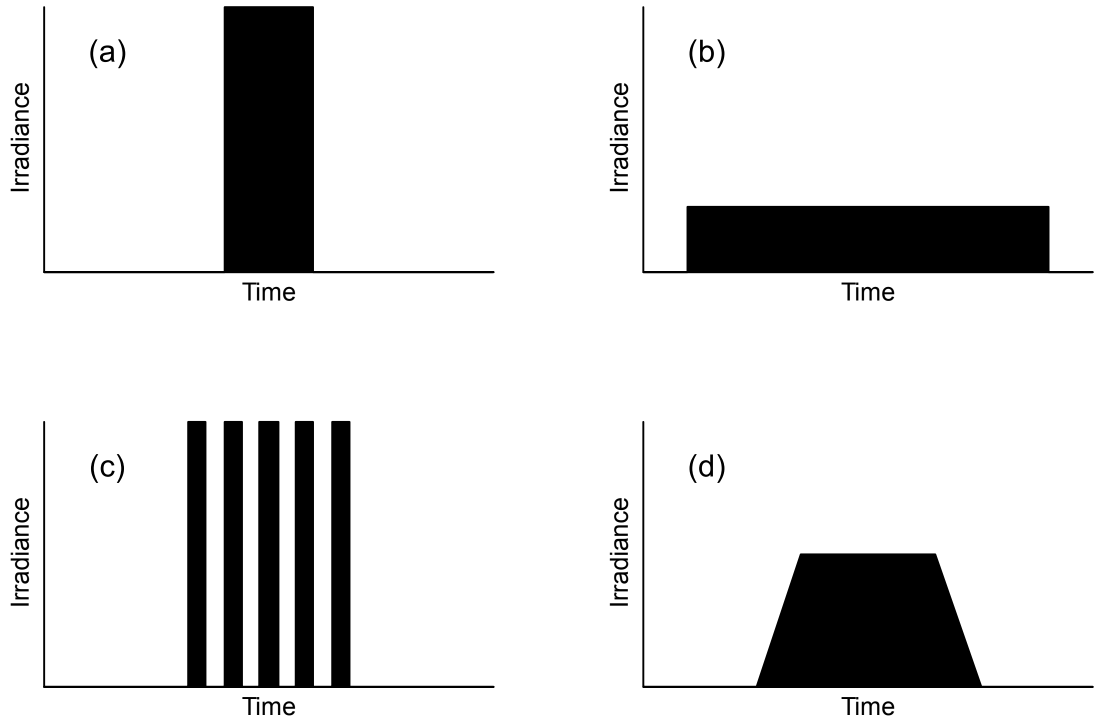
Experiments in which the photoresponse of a material is investigated as a function of radiant flux (dose rate or irradiance) are commonly called *reciprocity law experiments*. Bunsen and Roscoe (1859) are credited with conducting the first reciprocity law experiments. Reciprocity holds in photobiology when the observable response depends only on the total administered radiant exposure (commonly referred to as *dose*) and is independent of the two factors that determine total dose, that is, irradiance and exposure time.

Since the reciprocity law only depends on total dose, its validation for a particular end-point can have many experimental manifestations. Assuming that the reciprocity law is valid, then each manifestation should be equivalent to the others as long as the integrated total dose is the same. Thus, when the reciprocity law is obeyed, the same photobiological response is observed when specimens receive the same integrated total dose regardless as to whether the exposure is performed:

a) At a high irradiance for a short period of time.
b) At a low irradiance for a long period of time.
c) By repeatably switching a light source on-or-off and controlling both the on-off frequency of the light and the length of time that the light remains in the on-state and the off-state. Experiments in which the light is turned on-and-off at an extremely high frequency are called *flash photolysis experiments*, while experiments in which the light is turned on-and-off at a low frequency are called *intermittency experiments*.
d) By ramping the irradiance to a high level, holding the flux for a specified period of time, and then ramping it back down to a lower level or any variant of these stress regimes.

These exposure regimes, depicted graphically in Fig 3, are adapted from a similar representation given by Forbes et al (1979).

Figure 3: A selection of irradiance *vs* exposure time regimes for testing the law of reciprocity in which the integrated areas (i.e. dose) for each exposure regime are identical. When the reciprocity law is obeyed, the photoresponse for each of these exposure regimes is the same.
A summary of reciprocity experiments carried out in human and mouse skin are reviewed by Martin et al (2003). In every case, reciprocity for erythema was shown to hold. Of particular relevance to sunbed use, where exposure times will vary between a few minutes up to half-an-hour or so depending on the power and spectral output of the lamps, Meanwell & Diffey (1989) showed that exposure to polychromatic radiation for time periods ranging from 1s to 1h induced degrees of delayed erythema ranging from minimal to marked that depended only on dose and not dose rate. These findings both support and extend those of previous studies in which the end point was confined to minimal erythema.



(a) High UVR intensity over short period
(b) Low UVR intensity over long period
(c) High UVR intensity in short bursts
(d) Gradual increase, holding and decrease of UVR intensity

On the other hand, Table 2 shows that reciprocity has been shown not to hold in UV-induced mice skin carcinogenesis where, in general, for a fixed dose of UV radiation the carcinogenic effectiveness in mice skin increases as the irradiance decreases or is fractionated (van der Leun et al 2005).

Although reciprocity has been shown to hold for erythema, different skin types respond differently to repeated daily sub-erythemal doses of simulated solar UVR. In sun-sensitive skin types II these have a cumulative effect such that a frank erythema becomes evident after 2-3 exposures of 0.65MED (Sheehan et al, 2002). Whereas in sun-tolerant skin type IV, this accumulation is not observed which suggests much better resolution of acute UVR damage.

Table 2: UVR reciprocity studies in human and mouse skin. Mouse tumorigenesis studies are for SCC

Response	Source	Spectrum	Irradiation	Range in irradiance	Reciprocity?	Reference
Human skin						
Erythema	Mercury	Monochromatic	Continuous	4	Y	Hausser 1927
Erythema	Mercury	Monochromatic	Continuous	?	Y	Hausser 1928
Erythema	Mercury	Monochromatic	Continuous	8	Y	Luchiesh 1930
Erythema	Mercury	Monochromatic	Continuous	4	Y	Coblentz 1932
Erythema	Mercury	Monochromatic	Continuous	20	Y	Blum 1946
Erythema	Mercury	Monochromatic	Flash	200	Y	Schmidt 1963
Erythema	Mercury	Monochromatic	Continuous	10^3	Y	Park 1984
Erythema	Xenon	Monochromatic	Intermittent	?	Y	Everett 1969
Erythema	Xenon	Monochromatic	Continuous	?	Y	Everett 1969
Erythema	Xenon	Polychromatic	Continuous	10^3	Y	Meanwell 1989
Erythema	Laser	Monochromatic	Flash	3	Y	Parrish 1976
Erythema	Laser	Monochromatic	Continuous	10^4	Y	Anderson 1980
Langerhans cell depletion	Xenon	Monochromatic	Continuous	10	Y	Murphy et al, 1993
Mice skin						
Tumorigenesis	Mercury	Polychromatic	Continuous	12	N	Blum 1941
Tumorigenesis	Mercury	Polychromatic	Intermittent	4	N	Blum 1942
Tumorigenesis	Mercury	Polychromatic	Intermittent	4	N	Bain 1943
Tumorigenesis	Xenon	Monochromatic	Intermittent	3	N	Forbes 1979
Tumorigenesis	Fluorescent	Polychromatic	Continuous	5	N	Forbes 1981
Tumorigenesis	Fluorescent	Polychromatic	Continuous	8	N	de Gruijl 1983
Immunosuppression	Fluorescent	Polychromatic	Intermittent	1	Y	DeFabo 1979
Immunosuppression	Fluorescent	Polychromatic	Continuous	10	Y	DeFabo 1980
Immunosuppression	Fluorescent	Polychromatic	Continuous	10	Y	Noonan 1981

4 What are the specific health and safety implications (negative and positive) relating to the exposure of persons to UVR from tanning devices for cosmetic purposes?

4.1 Negative Effects

4.1.1. Acute and non skin cancer effects

The use of tanning devices has been associated with acute adverse reactions such as a form of skin fragility known as pseudoporphyria (Murphy et al, 1990; Weiss and Jung, 1990) and lentigines (Salisbury et al, 1989; Kadunce et al, 1990) that have been noted in case reports. There have also been case reports of induction (Fruchter and Edoute, 2004) and exacerbation (Stern and Docken, 1986) of systemic lupus erythematosus.

There is a risk of phototoxic reactions with people using certain medications (Bisland, 1990) or applying topical aromatherapy products, such as bergamot oil, that contain photosensitising chemicals (Kaddu and Wolf, 2001) or eating plants that contain such chemicals (Ljunggren, 1990).

Devices with a higher UVB/UVA ratio or a high UVB irradiance will be more effective at tanning and will require a shorter exposure time. However, this also increases the likelihood of a burn (doses > 1 MED) because there is a lower margin of error in the determination of exposure time (see Section 5). Burns have also been reported due to equipment failure (Eltigani and Mathews, 1994).

Studies in the late 1980s showed that the use of tanning devices has an adverse effect on human immune function (Hersey et al, 1987; Rivers et al, 1989). More recently, Whitmore and Morison (2000) reported that 10 full-body exposures over a two-week period suppressed immunity as assessed by the induction and elicitation arms of the contact hypersensitivity response (CHS). These authors also studied the effect of 10 full-body tanning exposures in 11 volunteers and, not surprisingly, reported the presence of CPD and p53 protein expression in keratinocytes *in vivo* (Whitmore et al, 2001). One study used a Cleo Natural source (see Figure 1) to assess the immunological effects of repeated whole-body sub-erythemal exposure (1.2 SED) on 165 skin types II and III for up to 30 consecutive days (Narbutt et al, 2005). The results showed a cumulative UVR dose-dependent reduction of the primary allergic response and the elicitation arm of the CHS response and suggest that there is no adaptation to these immunological responses.

Comment on UVA-induced immunosuppression
The role of UVB in immunosuppression is well established in mice and humans. The role of UVA is much less clear. Much of the evidence for the role of UVA in humans has come from sunscreen studies in which the addition of UVA filters has been shown to improve immunoprotection (Fourtanier et al 2005). In mice, there is evidence that UVA abrogates UVB-induced immunosuppression (Tyrrell and Reeve, 2006) but there is evidence of a positive interaction of UVB and UVA in human immunosuppression (Poon et al, 2005), i.e. the combined effect is greater than the sum of the parts. It should be noted that immunosuppression is a complex issue and that the above brief comments are a necessary simplification.

4.1.2 Chronic
Skin Cancer

Non-melanoma
Very few studies have been done on the relationship between sunbed use and non-melanoma skin cancer risk. Two hospital-based case-control studies in Ireland, in the mid to late 1980s, did not show any relationship between the use of tanning devices and non-melanoma skin cancer (O'Loughlin et al, 1985; Herity et al, 1989). A similar conclusion, at about the same time, was reached by Bajdik et al (1996) in British Columbia, Canada, who evaluated 406 controls (population based) against 180 SCC cases and 226 BCC cases. About 10% of each group had "ever" used a sunlamp. The adjusted OR for BCC and SCC for "ever" having used a sunlamp were 1.2 (0.7-2.2) and 1.4 (0.7-2.7) respectively, which are clearly non-significant. One small study from 2002, using the "generalized estimating equation method" reported no significant effect of tanning devices for BCC, even though the total lifetime exposure to tanning devices

was almost twice as high in patients compared with controls (Boyd et al, 2002). In the same year, Karagas et al (2002) assessed the relationship between use of tanning devices and BCC and SCC in a population-based case control study. In this study there was greater use of tanning devices ranging from 9.2% (male controls) to 28.4% (female patients). The OR for BCC and SCC were 1.5 (1.1-2.1) and 2.5 (1.7-3.8) respectively and adjustment for a variety of factors made no difference to these results. The results of Karagas et al (2002) indicated that the use of tanning devices is a risk factor for non-melanoma skin cancer.

Melanoma

Sunbed usage has increased considerably in recent years (Rafnsson et al, 2004) but the data on melanoma risk are scanty. There are a number of case-control studies but the details on exposure for the majority was small and all, as case-control studies, were subject to bias of recall and the effect of confounders. There is a single cohort study (Verierod et al, 2003) in which risk of melanoma was addressed.

A number of case-control studies reported no evidence of sunbed use as a risk factor for melanoma (Osterlind et al, 1988; Holly et al, 1995; Westerdal et al, 1994; Zanetti et al, 1988; Chen et al, 1998; Dunn-Lane et al, 1993; Naldi et al, 2000; Bataille et al 2004, 2005). The majority of these studies were, however, small and the prevalence of sunbed usage in cases and controls was very low. Others were supportive of weak evidence or evidence in "at risk" groups (Walter et al, 1990; Westerdahl et al, 2000). Walter et al (1990) showed some suggestion of a trend to increased risk of melanoma with longer duration of use. In the study by Westerdahl et al (2000) an increased risk of melanoma was demonstrated only for use of sunbeds before the age of 35 years (OR, 2.3; CI, 1.2–4.2). Swerdlow et al (1988) showed a significantly increased risk for any use of sunbeds OR 2.94 (95% CI 1.4-6.17) with a significant trend for increased duration of use. Autier et al (1994) showed little evidence of risk overall when corrected for skin type etc but did show evidence of increased risk for usage of sunbeds for 10 hours or more, when burning was reported after use of the sunbed or when the users reported use of the sunbed to tan.

The only cohort study to address risk associated with solaria followed more than 100,000 Norwegian and Swedish women for an average of 8 years, and 187 melanomas developed. This study identified use of a solarium for 1 or more times per month as a risk factor for melanoma. When the exposures occurred between the ages of 20 – 29 years the adjusted relative risk was 2.58 (95%CI 1.48-4.50). Among women who had used a solarium once or more per month, in at least one of the three decades between ages 10 and 39, the adjusted relative risk of melanoma compared to women that had never or rarely used a solarium during these three decades, was 1.55 (95%CI 1,4-2.32) (Veierød et al, 2003). This is probably the most persuasive evidence for a role for sunbeds in causing melanoma but the data are as yet relatively weak and support the view only that frequent use is deleterious.

Gallagher et al (2005) carried out a meta-analysis of 9 case-control studies and the one cohort study and came to the conclusion that sunbed use significantly increased the risk of melanoma with an OR of 1.25 (1.1-1.5) "ever" versus "never" used. This increased to 1.69 (1.3 –2.2) using the metric "first exposure as a young adult".

Photoageing
There seems to be no published literature on the photoageing effects of sunbed use but this would be expected from the long-term use of sunbeds because photoageing is associated with solar exposure (Fisher et al, 2002). Some studies have looked at the effect of repeated sub-erythemal exposure of UVB and UVA in human skin and reported some changes that are associated with photoageing (Lavker et al, 1995a, 1995b; Lavker and Kaidby, 1997).

As with the sun, tanning devices emit infrared radiation (IR: 760nm to 1mm). The effects of IR on skin are poorly understood but *in vitro* studies suggest that it may play a role in photoageing, which has been suggested by animal studies (Schieke et al, 2003).

Effects on the eye
Four studies have assessed the relationship between sunbed use and ocular melanoma and found varying degrees of association Tucker et al, 1985; Seddon et al, 1990; Holly et al, 1996). The most recent study (Vajdic et al, 2004) provides “moderately strong” evidence, with several metrics, that sunbed use results in ocular melanoma, after adjustment for confounding factors including exposure to solar radiation. The OR for use (never vs ever) was 1.7 (95% CI 1.0 – 2.8) and 2.4 (95% CI 1.0 – 6.1) for first use under 21 years. There was a significant trend ($p = 0.04$) for duration of use. This study also suggested a protective effect from wearing goggles with an OR = 2.2 (95% CI 0.5 - 9.7) in those who did not always wear goggles but this was not significant ($p = 0.3$).

4.2 Positive Effects

Vitamin D status
Tanning with UVB-emitting sunbeds would be expected to improve vitamin D status and this has been reported in a recent study (Tangpricha et al, 2004) that showed that people who used a sunbed at least once a week for at least 6 months had a mean serum concentration of 25 hydroxyvitamin D (25(OH)D) of 115.5 ± 8.0 (SEM) nmol/L compared with the controls who had levels of 60.3 ± 3.0 nmol/L ($P < 0001$). The tanners also had significantly higher hipbone mineral density. However, this study has several flaws; (i) it relied on recall of sunbed use without establishing serum 25(OH)D before sunbed use, (ii) the tanning group had much greater sunlight exposure and (iii) there was a much greater proportion of white-skinned people in the tanning group. Furthermore, there were no data on the spectral output of the tanning devices used.

Feel good factor
Many people claim to feel better after sunbed use (Diffey 1986) but studies using primarily UVA emitting sunbeds showed that mood effects could not be attributed to circulating serotonin or melatonin (Gambichler et al, 2002a) or opioid peptides (Gambichler et al, 2002b). The possible role of UVB-induced keratinocyte-derived β-endorphin (Gilchrest et al, 1996) has yet to be investigated.

5. (a) Are limit values necessary for the irradiance of UVR from artificial sources, in particular from tanning devices for cosmetic purposes, with respect to health and safety? (b) Is it necessary to give different values for the irradiance of UVA, UVB and UVC radiation respectively? (c) If so, please specify the limit values for the irradiance of artificial UVR above which adverse health effects will occur. What are the uncertainties of these limit values?

From the above discussion on reciprocity, it is clear that acute clinical effects resulting from sunbed use (i.e. erythema) are likely to depend only on total dose and not dose rate. It is not possible to make any statements on the risk of skin cancer, especially melanoma. Since all tanning devices emit a broad UVR spectrum, the spectral profile of which determines the device's effectiveness to elicit clinical effects, it is irrelevant to specify irradiance limits in different spectral wavebands, especially since the spectral regions UVA, UVB and UVC were originally based on the optical properties of different glasses (see section 2b). A more appropriate way to speak of tanning devices than using the terms UVA, UVB and UVC is to compare their erythemal power, as a percentage of total UVR power, with sunlight. This is expressed mathematically as:

$$100 \times \sum_{290}^{400} E(\lambda).\varepsilon(\lambda).\Delta\lambda \,/ \sum_{290}^{400} E(\lambda).\Delta\lambda$$

E(λ) is the relative spectral power distribution of the UV source and *ε(λ)* is the erythemal effectiveness of radiation of wavelength λ nm (CIE 1998). An example of this calculation is given in Appendix A. For the 3 sources illustrated in the Figure 1, the erythemally effective percentages are 0.44%, 0.51% and 0.13% and for summer sunlight, the "Cleo Natural" and "Cleo Performance" lamps, respectively. Clearly, the "Cleo Natural" lamp more closely resembles sunlight "biologically" than the "Cleo Performance" lamp.

In specifying an upper limit of irradiance, the important quantity is the erythemally-weighted irradiance, obtained by weighting each spectral irradiance component of the lamp by its relative effectiveness to induce erythema and summing over all wavelengths present in the source spectrum (see equation above). To minimise the risk of timing errors, which might result in "sunburn" it is desirable that the prescribed sunbed exposure session should be no less than 10 minutes. The avoidance of "sunburn" may also reduce the risk of melanoma.

Depending on an individual's phototype, the exposure in SED during this 10-minute period should not exceed the subject's estimated indicative MED (see Table 1). The maximum erythemal-weighted irradiance should not exceed 11 SED/h (0.3 W/m^2). This is equivalent to a UV index (UVI) of 12, which WHO describes as "extreme". A noon UVI of 12 would be typical in summer in Darwin, Australia (13^oS) and Colombo, Sri Lanka (13^oN).

The main conclusion from this analysis is that the erythemally weighted properties of a given sunbed emission spectrum (as demonstrated in Appendix A) are more important than its physical properties *per se*. This is because UVB is orders of magnitude more erythemogenic than UVA (as shown in Figure 2) which, as shown in Figure 1, is the main UVR component of sunlight and tanning device spectra. At present, certainty can only be reasonably assured for acute effects such as erythema.

6 Please specify the limit values of total dose of artificial UVA, UVB and UVC radiation above which adverse health effects will occur, taking into account skin phototype, intensity of exposure, duration of exposure and associated uncertainties.

The clinical effects of UVR exposure can be either *deterministic*, where the magnitude of the effect is related to exposure and a threshold dose is possible, or *stochastic,* in which the probability of the effect is related to exposure and there is no threshold dose. Erythema is an example of a deterministic effect with a threshold and SCC is a stochastic effect without a threshold.

There is no need to specify total dose separately for UVA, UVB and UVC for the reasons given in Section 5. It is not possible to specify uncertainties for long-term effects.

For a single exposure on a sunbed it is important to avoid marked or severe erythema but necessary (for the desired cosmetic effect) to receive a sufficient UVR dose to stimulate melanogenesis. Experience has shown that an exposure at or just below that to induce a just perceptible MED 8 to 24 hours after exposure approximates the optimum.

A classification of skin phototypes based on susceptibility to sunburn in sunlight (WHO 2003), together with indicative MEDs that might be expected following exposure on unacclimatized skin, is given in Table 1. Depending on an individual's phototype, the exposure in SED on any single occasion should not exceed their estimated indicative MED.

With a stochastic effect like SCC skin cancer there is no threshold dose below which the effect will not occur. Consequently, any recommendation about a limit value of total dose accumulated over a specific time period (e.g. year, lifetime) is arbitrary and subjective. A limit of 20 sessions per year (equivalent to an exposure of approximately 40 SED or 20 MED in melano-compromised individuals) was proposed by the British Photodermatology Group (BPG) in 1990 (Diffey *et al* 1990) and was subsequently adopted by the UK Health & Safety Executive (HSE 1995).

The International Electrotechnical Commission (1995) recommends that the maximum annual exposure should not exceed an erythemal-weighted dose of 15 kJ/m^2 (150 SED), equivalent to around 50 MED in white-skinned people. Not surprisingly, it is this higher limit adopted by The Sunbed Association in the UK in their code of practice for operators (TSA 2004). A pragmatic defence of the limit of 20 sessions per year is that it discourages people from purchasing sunbeds to use at home where the temptation to use them several times a week or for prolonged time during a single tanning session is evident.

Other agencies have simply advised against sunbed use and not specified an "acceptable" maximum annual usage (AGNIR 2002; WHO 2003; ICNIRP 2003).

Estimates have been made of the risk of basal and squamous cell skin cancers arising from sunbed use (AGNIR 2002) and what constitutes an "acceptable" risk is a matter of judgment. For most people, who may use sunbeds 10 or 20 times a year for 10 years or so in young adulthood, the estimated additional lifetime risk of non-melanoma skin cancer, compared with non-users, is up to 10% (AGNIR 2002).

Case-control studies, particularly more recent ones, have generally found an association between sunbed use and melanoma (Young 2004) with an odds ratio of around 1.5 (Veierød et al. 2003). In communicating this risk to policy makers (Heller *et al* 2003), it may be helpful to estimate the potential number of cases and deaths prevented each year in a population if sunbeds were eliminated. These are given in Table 3 for the UK, where the relative risk of incidence and mortality of sunbed users is taken to be 1.5 relative to non-users. The figure of 1.5 is used for illustrative purposes since different studies have yielded different relative risks (Young 2004) and so the population impacts in Table 3 should be treated with caution (B. Diffey). Melanoma incidence and mortality data refer to the year 2002 (Cancer Research UK, 2005).

Sex	Millions in UK Population in 2002	Melanoma per 10^5		% using sunbeds	Relative risk of incidence & mortality	Population attributable risk	No. affected in 2002?		Estimated population impact (no. people) by eliminating sunbeds	
		Incidence	Mortality				Incidence	Mortality	Incidence	Mortality
Male	28.7	11.2	3.0	5	1.5	0.024	3193	874	78	21
Female	30.3	13.7	2.5	9	1.5	0.043	4128	770	179	33
						Total	**7321**	**1644**	**257**	**54**

Table 3 Non-use of tanning devices might have resulted in about 54 fewer deaths from melanoma in 2002 than the 1644 that were observed in the UK

An alternative approach to estimating the mortality associated with sunbeds is through modelling population exposure to both sunlight and sunbeds, assuming that the patterns of exposure from these two sources are equally carcinogenic, that the melanomas that result are equally fatal, and that the fraction of deaths due to sunbed use is equal to the population exposure from sunbeds expressed as a fraction of the total population exposure from sunlight and sunbeds. Using this approach Diffey (2003) estimates the mortality due to sunbed use each year in the UK is around 100, with a range of about 50 to 200. The estimates from this approach and that illustrated in Table 3 are not inconsistent given the many uncertainties and assumptions involved. If it is assumed that the use of sunbeds increased the risk of melanoma by 50%, the additional lifetime risk of dying from melanoma will be of the order $1x10^{-3}$. From the above discussion it is clear that there is no limit value of total dose of artificial UVR below which adverse health effects will not occur and that any limit is subjective and arbitrary.
Based on data available the risk of developing skin cancer in connection with the use of sunbeds is high in comparison to the "acceptable" risk of developing cancer from other consumer products (WHO, in press).

4. COMMENTS RECEIVED DURING THE PUBLIC CONSULTATION

23 comments were received mainly from public health bodies and the sunbed industry. Some from public health bodies felt the SCCP committee had not sufficiently emphasized the health risks of sunbed use and those from industry felt that we had made too much of these risks. Some comments from public health bodies were accompanied with their own documents on the risks of UVR including that from sunbeds. There were several comments on vitamin D, some stating that there was no evidence of benefits other than for skeletal health and others stating that these benefits were better established than we had stated. Overall, there were many comments on detail, some of which have been addressed but none of which alters the overall conclusions of the SCCP committee.

There were a few common themes in the comments that we have specifically addressed:

- The erythemally weighted irradiance limit that was originally given was too high and we have now reduced this to $0.3W/m^2$ which is in accord with other bodies
- There was no discussion on the effects of UVR on melanoma of the eye. This has now been addressed along with the inclusion of a study that shows a relationship between sunbed use and melanoma of the eye.
- The lack of inclusion of CIE action spectra that have now been included in Figure 2.

Comments received:

- Afsse (Agence Française de Sécurité Sanitaire Environnementale), InVS (Institut de Veille Sanitaire), afssaps (Agence Française de Sécurité Sanitaire des Produits de Santé)
- Afsset (Agence Française de Sécurité Sanitaire de l'Environnement et de Travail)
- BEUC, the European Consumers' Organisation
- The British Medical Association
- Cancer Research UK
- Dr. Jean-Pierre Cesarini, France
- Charité – Medical University, Germany
- Ir. G. Crevecoeur, Belgium
- Dr. Jan C. van der Leun (Ecofys BV, the Netherlands) and Dr. Paul Donald Forbes (Toxarus, Inc., USA)
- European Sunlight Association, Belgium
- EUROSKIN (European Society of Skin Cancer Prevention), Germany
- Gezondheidsraad / Health Council of the Netherlands
- UK Health Protection Agency
- Dr. Ph. Autier, France
- Bayerisches Staatsministerium für Umwelt, Germany
- Dr. Nji Ousseni, France
- State Non-Food Products Inspectorate, Lithuania
- Public Health Authority, Slovakia
- Nordic Radiation Protection and Health Authorities
- Dr. Alexander Steinmann, Germany
- SUNARC, USA

- Dr. Paul Donald Forbes (Toxarus, Inc., USA)
- Hospital Universitario de la Princesa, Spain

5. CONCLUSION

Question 1: What are the general health and safety implications (negative and positive) relating to the exposure of persons to ultraviolet radiation (UVR)[7]?

- Clinically relevant UV-radiation is UVB (280 – 315 nm) and UVA (315-400 nm)
- Solar UVB (~295 – 315nm) is primarily responsible for inducing erythema (sunburn) and tanning
- UVA has similar acute clinical effects to UVB if the physical doses (J/cm^2) given are approximately 1000 times greater
- Human skin may be phenotypically classified into phototypes I – VI which are determined by acute sensitivity to sunlight, melanin content and tanning ability
- Solar exposure is associated with basal cell carcinoma, squamous cell carcinoma and malignant melanoma.
- The risk of a given type of skin cancer is influenced by patterns of UVR exposure
- Phototype is a good indicator of skin cancer risk which reflects acute sensitivity to sunlight with phototype I being the most sensitive and phototype VI being the most resistant
- Moles and freckles are good indicators of susceptibility to malignant melanoma
- Moles and freckles are independent risk factors for skin cancer
- UVR is immunosuppressive in humans, the consequences of which are unknown but may be important in skin cancer and infectious diseases
- Public health messages should be directed to those people at greatest risk of skin cancer in order to promote behaviour which is appropriate to the balance of risk
- Solar UVR, especially UVB, causes photokeratitis (snow blindness) of the eye and increases a cataract formation.
- There is evidence that solar UVR exposure is associated with ocular melanoma

Question 2: What are the differences between risks associated with exposure of persons to natural UVR and those risks from artificial UVR? What are the differences regarding the health and safety risks with respect to exposure of persons to UVA, UVB and UVC radiation respectively?

- There are no intrinsic differences between the physical and biological properties of natural and artificial UVR but there are differences in spectral profile that may have biological consequences

[7] The International Commission on Illumination (CIE) defines ultraviolet radiation (UVR) as optical radiation between 100 and 400 nm. The spectral region is divided into three photo-biological spectral regions: UVC (l00-280 nm), UVB (280-315 nm) and UVA (315-400 nm).

- It is relatively easy to compare the acute effects of natural and artificial UVR but much more difficult to compare the long-term effects.
- UVR, with and without photosensitizers, is used in the phototherapy of skin diseases and skin cancer is an accepted risk in such treatment
- Wavelength dependency (action spectrum) studies show that UVB is the most harmful part of the solar UVR spectrum for both acute and long term term-effects but wavelength dependency data on UVA are more limited than for UVB
- We lack data to make conclusive statements on the wavelength dependency of melanoma

Question 3: Is the total dose value of UVR the only effective health and safety parameter with regard to the risks associated with exposure of persons to both natural and artificial UVR? What is the validity of the Bunsen-Roscoe law[8] over the range of irradiances and wavelengths associated with exposure of persons to both natural and artificial UVR?

- The reciprocity law applies for human erythema
- There are no quantitative human data for long-term effects but patterns of exposure may be important, especially for melanoma (see Question 1) that suggests a failure of the reciprocity law

[8] The Bunsen-Roscoe law (law of reciprocity) states that a certain biological effect is directly proportional to the total energy dose irrespective of the administered regime. Dose is the product of intensity and the duration of exposure. (Bunsen R, Roscoe HE, Photochemische Untersuchungen, Poggendorff˝s Annalen 1855: 96: 373-394, 1857: 100: 43-88 and 481-516, 1857: 101:235-263, 1859: 108: 193-273.).

Question 4: What are the specific health and safety implications (negative and positive) relating to the exposure of persons to UVR from tanning devices for cosmetic purposes?

- There are some case reports for adverse clinical effects (other than skin cancer) from sunbed use but it is not possible to estimate the frequency of these
- Several studies, and a meta-analysis, have shown a significant association between sunbed use and malignant melanoma. Typically, the risk for developing melanoma in relation to the use of sunbeds is around 1.5.
- Sunbed use can result in the desired cosmetic outcome which is tanning
- There is no evidence to support a pharmacological basis for the "feel good" factor of sunbed use
- Use of sunbeds that contain UVB may enhance vitamin D status but there are few data available on this relationship. The emission spectrum of the source is likely to be important
- There is some evidence that sunbed use is associated with ocular melanoma

Question 5: Are limit values necessary for the irradiance of UVR from artificial sources, in particular from tanning devices for cosmetic purposes, with respect to health and safety? Is it necessary to give different values for the irradiance of UV-A, UV-B and UV-C radiation respectively? If so, please specify the limit values for the irradiance of artificial UVR above which adverse health effects will occur. What are the uncertainties of these limit values?

- The biological consequences of a given sunbed emission spectrum are much more relevant than its specific irradiances within different wavebands which were originally defined by physical rather than biological parameters
- A biologically effective dose can be obtained by weighting a given emission spectrum with a relevant action spectrum
- This weighting should be done with the human erythema action spectrum, which is similar to the tanning action spectrum and the estimated human action spectrum for squamous cell carcinoma. This gives an erythemally weighted irradiance of the emission spectrum of the sunbed as demonstrated in Appendix A
- The maximum erythemally weighted irradiance should not exceed 0.3W/m2, or 11 standard erythema doses (SED) per hour. This is equivalent to tropical sun, which the WHO terms extreme.
- Certainty can only be reasonably assumed for acute effects

Question 6: Please specify the limit values of total dose of artificial UV-A, UV-B and UV-C radiation above which adverse health effects will occur, taking into account skin phototype, intensity of exposure, duration of exposure and associated uncertainties.

- There is no need to specify different dose limits for UVB and UVA for the same reasons given in Question 5. However, there is no justification for the presence of UVC in tanning devices.
- The dose limits for adverse acute effects are dealt with in Question 5. In the context of risk assessment, it is not possible to give dose limits for skin cancer because of lack of

human dose-response data. However, SCC is a stochastic effect for which there is no assumed threshold dose. Any annual dose limits given are arbitrary

- The human erythema action spectrum is similar to the estimated human SCC action spectrum based on mouse data. This may also represent the wavelength dependency for human BCC. However, we lack mammalian data on the wavelength dependency of malignant melanoma. Broad spectrum studies in mice indicate that as with non melanoma skin cancer, UVB is much more important than UVA
- The important biological risk factors for malignant melanoma are age, sex (in some populations), skin phenotype (in particular types I and II), moles, freckles and family history. Behavioural/environmental risk factors include intermittent sunburning UVR exposure, especially in youth.
-

Overall Conclusion

UVR tanning devices were not in widespread use before the 1990-s and the full health effects of their use are not yet known. It will take several years before the real picture of the role of the UVR tanning devices in inducing skin cancer becomes fully apparent. This is due to the long induction period of the cancer.

The SCCP is of the opinion that the use of UVR tanning devices to achieve and maintain cosmetic tanning, whether by UVB and/or UVA, is likely to increase the risk of malignant melanoma of the skin and possibly ocular melanoma.
People with known risk factors for skin cancer, especially malignant melanoma, should be advised not to use UVR tanning devices. Specifically, these are (i) skin phototypes I and II and the presence of freckles, (ii) atypical and/or multiple moles and (iii) a family history of melanoma. Eye protection from UVB and UVA should be worn if sunbeds are used.

Risk of melanoma seems to be particularly high when using sunbeds at a young age. Thus UVR tanning devices should not be used by individuals under the age of 18 years.

6. MINORITY OPINION

Not applicable

7. GLOSSARY

AK – actinic keratosis
BCC – basal cell carcinoma
BPG – British Photodermatology Group
CHS – contact hypersensitivity
CI – confidential interval
CIE - Commission Internationale de l'Éclairage
CPD – cyclobutane pyrimidine dimers

IARC – International Agency for Research on Cancer
IPD – immediate pigment darkening
IR – infrared radiation
LVD - Low Voltage Directive
MED – minimal erythema dose
MMP – matrix metalloproteinases
PUVA – psoralen plus UVA
OR – odds ratio
RR – relative risk
ROS – reactive oxygen species
SCC – squamous cell carcinoma
SCCP – Scientific Committee on Consumer Products
SED – standard erythema dose
SPF – sun protection factor, based on UVB absorbance
SSR – solar simulating radiation
UCA – urocanic acid
UVA –Ultraviolet radiation with wavelengths 380–315 nm
UVA-I –Ultraviolet radiation with wavelengths 340-400m
UVA-II –Ultraviolet radiation with wavelengths 315-340nm
UVB - Ultraviolet radiation with wavelengths 315–280 nm
UVC - Ultraviolet radiation with wavelengths < 280 nm
UVR - ultraviolet radiation
XP – xeroderma pigmentosum

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10. APPENDIX A: TECHNIQUE FOR DETERMINING THE ERYTHEMAL-WEIGHTED IRRADIANCE

The erythemal-weighted irradiance should be determined by means of a calibrated spectroradiometer. This type of measurement, known as spectroradiometry, enables the intensity of UV radiation on a wavelength-by-wavelength step to be recorded over all the wavelengths present in the sunbed emission spectrum. A spectroradiometer is an expensive, complex piece of optical equipment, which is found mainly in laboratories with a special interest in photobiology. It is important that users of spectroradiometers have their own standard lamps (either deuterium or tungsten) regularly calibrated by a national standards laboratory so that these can be used to provide an absolute spectral sensitivity calibration of the spectroradiometer.

The technique is to place the input optics of the spectroradiometer on top of the plastic sheet of the sunbed or at the recommended tanning distance from a sun canopy. The spectral irradiance is measured in equal wavelength steps (e.g. 5nm) from 280 to 400nm resulting in a set of numbers like those shown in column 2 in the table below. The numbers in column 3 represent the erythema action spectrum. This is the relative effectiveness of UV radiation of different wavelengths to cause erythema (or redness) in human skin 8-24 hours after exposure. The numbers in each row of columns 2 and 3 are multiplied together in column 4. All the numbers in column 4 are summed to give (in this example this comes to 0.0355) and then multiplied by 5nm (the wavelength interval used in scanning the spectrum) to give the erythemal-weighted irradiance in W/m^2, which in this example is 0.0355 x 5 = 0.18 W/m^2. This number should not exceed 0.3 W/m^2.

nm	Spectral irradiance $W/m^2/nm$	erythema action spectrum	Erythemal weighted irradiance
280	0.00	1	0.0000
285	0.00	1	0.0000
290	0.00	1	0.0000
295	0.00	1	0.0000
300	0.00	0.64863	0.0000
305	0.01	0.21979	0.0015
310	0.03	0.0745	0.0020
315	0.11	0.0252	0.0029
320	0.32	0.00855	0.0027
325	0.76	0.0029	0.0022
330	1.51	0.00136	0.0020
335	2.44	0.00115	0.0028
340	3.35	0.00097	0.0032
345	4.08	0.00081	0.0033
350	4.71	0.00068	0.0032
355	4.83	0.00058	0.0028
360	4.48	0.00048	0.0022
365	5.57	0.00041	0.0023
370	3.09	0.00034	0.0010
375	2.27	0.00029	0.0007
380	1.52	0.00024	0.0004

nm	**Spectral irradiance W/m^2/nm**	**erythema action spectrum**	**Erythemal weighted irradiance**
385	0.98	0.0002	0.0002
390	0.70	0.00017	0.0001
395	0.44	0.00015	0.0001
400	0.28	0.00012	0.0000
		Sum	**0.0355**