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Norwegian Scientific Committee for Food Safety

Opinion of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of the Norwegian Scientific Committee for Food Safety

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Risk assessment related to solar radiation and the use of sun protection products

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SUMMARY

The European Commission has recently established recommendations to ensure that sunscreen products manufactured and sold on the European market provide a minimum degree of protection against UVB- and UVA-radiation. The Norwegian Food Safety Authority would like to have an inclusion of these new recommendations for sunscreen products in the regulation of cosmetic products. They have therefore asked the Norwegian Scientific Committee for Food Safety four questions which have been answered as follows:

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

Clinically relevant UVR from exposure to solar radiation is UVB (280 – 320 nm) and UVA (320 – 400 nm). UVB penetrates down to only a few micrometers and is primarily responsible for inducing erythema (sunburn) and tanning while UVA can go through the epidermis and irradiate underlying tissues. The internationally agreed UV-index is defined in terms of the erythemally weighted irradiance and is intended for use as for information purposes towards the general public. Human skin may be phenotypically classified into phototypes I – VI according to acute sensitivity to sunlight, melanin content and tanning ability. Solar exposure is associated with basal cell carcinoma, squamous cell carcinoma and malignant melanoma. The phototype is a good indicator of skin cancer risk, phototype I being the most sensitive and phototype VI being the most resistant. Moles and freckles are good indicators of susceptibility to malignant melanoma. Exposure of the skin to solar radiation results in skin ageing and is immunosuppressive. Solar radiation causes photokeratitis (snow blindness) of the eye and contributes to cataract formation. There is evidence that solar UVR exposure is associated with ocular melanoma. Sun exposure is the most important source of vitamin D formation in human.

2. What are the specific health and safety implications (negative and positive) relating to the use of sun protection products during exposure of persons to solar radiation?

Public health programs aimed at preventing skin cancer focus on protection from sunlight. They incorporate a range of strategies, including using broad-spectrum sunscreens. Sunscreens were first developed to protect against sunburn and were designed to filter out UVB. More recently, substances that filter out UVA have also been added to sunscreens. The sun protection factor (SPF) indicates protection against UVB. No internationally harmonized method for determination of UVA protection is available. The *in vivo* Persistent Pigment Darkening (PPD) method is proposed to be used in the EU to indicate UVA protection. The critical wavelength method evaluates the uniformity of the absorption spectrum of a sunscreen. Before UV screens are put on the marked within EU, the Scientific Committee on Consumer Products evaluates them for safety. A potentially estrogenic effect of some UV-filters has been claimed. The Scientific Committee on Cosmetic and Non-Food Products has concluded that organic UV filters used in cosmetic sunscreen products allowed in the EU market today, have no estrogenic effects that could potentially affect human health. Sun protection products offer real, documented effectiveness in preventing sunburn. Sunscreens with high protection indices for UVB and for UVA-radiation provide effective protection against the decrease in cellular immune reactions. Sunscreens probably prevent squamous cell carcinoma in the skin. No conclusion can be drawn about the cancer preventive activity of topical use of sunscreens against basal cell carcinoma and cutaneous melanoma. It should be noted that the majority of the studies may have been carried out on populations that may have used sunscreens providing inadequate protection against UVA. Since the main purpose of sunbathing is to obtain a tan, and much higher sun exposure is needed to obtain a tan than to obtain an adequate vitamin D level, it follows that even the use of sunscreens with high SPF during sunbathing will give an adequate vitamin D level.

3. When and where are sun protection products used? How much and what type of sunscreen products are used?

Unprotected risk behavior (e.g. sunbathing or exposing shoulders without sun protection) occurs both among children and adults. The average amount of topical sunscreen applied (0.5 or even 0.25 mg/cm^2) is found to be far below the amount recommended for the technical evaluation of protection factor (2 mg/cm^2), thus the average protection is probably only 1/3 of the SPF given for the sunscreen

used, assuming that there is a linear relationship between thickness of sunscreen and protection. If there is an exponential relationship the protection will only be about 13% of the SPF given. Thus, studies are needed to establish the relationship between the thickness of sunscreen applied and the resulting sun protection. Moreover the amounts used at different sites of the body may vary between 0 and 1.2 mg/cm^2. A large number of sunbathers experience sunburn. This may in part be due to unprotected risk behavior and in part to differences in the thickness of the sunscreen applied at different sites.

4. Are specific limit values of sunscreen protection factors to solar radiation necessary? Is it necessary to give different values for the protection factors of UVB and UVA? Give the rational for the proposed values.

As late as in 2006, a Norwegian study of 15 different sunscreen preparations revealed that 3 of the products (20%) only gave little or no UVA protection. Six of the products tested (40%) did not satisfy the EU Commission recommendation on the efficacy of sunscreen products. These results clearly demonstrate the need for a stronger regulation of the sunscreen market. Numerical labeling of sun protection products with SPF should be discontinued as it has led to more confusion than clarity. Instead the products should have qualitative messages which focus on protection. Sun protection products should be labeled as providing low, medium, high, or very high protection. In terms of public health, it is important to raise public awareness of potential adverse health effects from sunbathing. Adults in strong sunshine (UV-index ≥ 4) should be encouraged to use high or very high protection sunscreens. Parents should be encouraged to let their children use high or very high protection sunscreens under conditions with UV-index ≥ 3. Products with SPF for UVB protection of less than 6 should not be classified as sun protection products as they do not provide any practical protection. With regard to UVA, the Council of Europe and the EU Commission recommendation recommend that the PPD/SPF ≥ 1/3. The value of the critical wavelength should exceed 370 nm in order to be accepted as a "broad-spectrum" sunscreen.

RECOMMENDATIONS

1. *The Sun Protection Factor (SPF) determined in vivo (Colipa 2006) should be used as indicator for UVB protection.*
2. *The persistent pigment darkening (PPD) determined in vivo should be used as indicator for UVA protection.*
3. *The persistent pigment darkening (PPD) determined in vivo should be further developed with the aim of obtaining an international agreement for the method and the analytical procedure.*
4. *The term "sun protection products" and similar terms indicate that the product protects both against UVB and UVA. The protection against UVB should correspond to SPF ≥ 6. The protection against UVA should correspond to the ratio PPD/SPF ≥ 1/3, and the value of the critical wavelength exceeding 370 nm.*
5. *The following terms should be used to indicate the protection against erythema: Low protection (6.0 ≤ SPF ≤ 14.9); Medium protection (15.0 ≤ SPF ≤ 29.9); High protection (30.0 ≤ SPF ≤ 59.9); Very high protection (60.0 ≤ SPF).*
6. *Studies are needed to establish the relationship between thicknesses of sunscreen applied and sun protection.*
7. *It is desirable to develop internationally harmonised in vitro methods for determination of sun protection.*

NORWEGIAN SUMMARY
SAMMENDRAG

I september 2006 kom EU-kommisjonen med anbefalinger som skal sikre at solkrem som blir produsert og solgt på det europeiske markedet, skal gi en faktisk beskyttelse mot UVB- og UVA-stråling som ligger over et visst minimumskrav. Mattilsynet vil arbeide for å få kommisjonens nye anbefalinger for solkrem inkludert i regelverket for kosmetikk og kroppspleieprodukter, slik at de blir rettslig bindende. De har derfor bedt om en vitenskapelig vurdering fra Vitenskapskomiteen for Mattrygghet (VKM) basert på fire spørsmål som er besvart som følger av Faggruppen for tilsetningsstoffer, aroma, matemballasje og kosmetikk:

1. Hva er de generelle helsemessige og sikkerhetsmessige konsekvenser (negative og positive) relatert til personers eksponering for UV-stråling?
UVB-stråler (280-320 nm) trenger bare noen få mikrometer ned i huden og er primært forbundet med dannelse av erytem (solforbrenning) og pigmentering (bruning), mens UVA-stråler (320-400 nm) kan trenge gjennom epidermis (overhuden) og bestråle underliggende vev. Den internasjonalt aksepterte enheten UV-indeks er en verdi som angir styrken på solens UV-stråler (erytemal bestråling), og den er ment å være et enkelt informasjonsverktøy for den generelle befolkningen. Huden kan klassifiseres fenotypisk i hudtype I – VI, i henhold til akutt følsomhet for sollys, melanininnhold og evne til å oppnå brunfarge. Soleksponering er forbundet med basalcellekarsinom, plateepitelkarsinom og malignt melanom (føflekkreft). Hudtype fungerer som en god indikator for utvikling av hudkreft, hvor personer med hudtype I er mest sensitive, og personer med hudtype VI er mest motstandsdyktige. Føflekker og fregner er gode indikatorer for følsomheten for å utvikle malignt melanom. Eksponering av huden for solstråling kan resultere i aldring av huden og svekkelse av immunsystemet. Solstråling kan forårsake fotokeratitt (snøblindhet) i øyet og øke dannelsen av katarakt. Det er holdepunkt for at UV-stråling fra sola er forbundet med okulært melanom. Soleksponering er den viktigste kilden for dannelse av vitamin D i kroppen.

2. Hva er de spesifikke helsemessige og sikkerhetsmessige konsekvensene (negative og positive) relatert til personers bruk av solbeskyttelsesmidler mot eksponering for UV-stråling?
Folkehelseprogrammer for forebygging av hudkreft fokuserer på beskyttelse mot solstråling. De omtaler en rekke forebyggende strategier, herunder bruk av bredspektrede solkremer. Solkremer ble først utviklet for å beskytte mot solbrenthet, og produktene ble da utformet for å filtrere UVB-stråler. I den senere tiden, har også ingredienser som beskytter mot UVA-stråling blitt tilsatt i solkrem. Solbeskyttelsesfaktoren (solfaktoren, SPF) angir beskyttelsen mot UVB-stråling. Det finnes per i dag ingen internasjonalt harmonisert metode for bestemmelse av UVA-beskyttelse. Metoden som er basert på *in vivo* "Persistent Pigment Darkening" (PPD) er foreslått brukt i EU for å angi beskyttelsen mot UVA-stråling. Kritisk bølgelengde beskriver absorpsjonsspekteret til en solkrem og sier noe om hvorvidt produktet gir en bredspektret beskyttelse. UV-filtre blir sikkerhetsvurdert av EUs vitenskapelige komité for forbrukerprodukter (SCCP) før de tillates brukt i produkter på det europeiske markedet. Det har vært hevdet at noen UV-filtre kan ha en østrogen lignende effekt. EUs vitenskapelige komité for kometikk og ikke-matvare produkter (SCCNFP) har konkludert med at organiske UV-filtre som brukes i solkremer som tillates på det europeiske markedet i dag, ikke har noen østrogen effekt som potensielt skulle kunne påvirke helsen. Det er dokumentert at solbeskyttelsesmidler effektivt forbygger solbrenthet. Solkrem med en høy grad av beskyttelse mot UVB- og UVA-stråling gir effektiv beskyttelse mot en nedgang i cellulære immunreaksjoner. Solkrem forebygger sannsynligvis utviklingen av plateepitelkarsinom i huden. Det kan ikke trekkes noen sikre konklusjoner om hvorvidt solkrem virker

forebyggende på utviklingen av kreftformene basalcellekarsinom og hudmelanom. I denne sammenheng er det imidlertid viktig å være oppmerksom på at flertallet av relevante studier kan ha blitt utført på befolkningsgrupper som har benyttet solkrem med utilstrekkelig beskyttelse mot UVA-stråling. Siden hovedhensikten med å sole seg er å bli brun, og det kreves en mye høyere soleksponering for å få en brunfarge enn å oppnå et tilstrekkelig vitamin D-nivå, vil selv bruk av solkrem med en høy solfaktor kunne gi et tilstrekkelig vitamin D-nivå.

3. Hvor og når blir solbeskyttelsesmidler benyttet? Hvor mye og hvilken type solkrem blir brukt?
Ubeskyttet soleksponering (f.eks soling eller eksponering av skuldre uten solbeskyttelse) forekommer både hos barn og voksne. Mengden solkrem som en person i gjennomsnitt smører seg inn med (0,5 eller så lite som 0,25 mg/cm^2) er funnet å være langt under den mengden som anbefales for teknisk fastsettelse av et produkts solfaktor (2 mg/cm^2). Hvis det antas at det er et lineært forhold mellom tykkelse av påført solkrem og beskyttelse, vil derfor den gjennomsnittlige beskyttelsen trolig bare være 1/3 av den solfaktoren som er angitt på produktet. Hvis det er et eksponentielt forhold, vil beskyttelsen bare utgjøre 13% av den angitte solfaktoren. Det er derfor nødvendig med flere studier for å nærmere kunne avklare forholdet mellom tykkelse av påført solkrem og den solbeskyttelsen dette vil gi. Videre er det vist at mengden solkrem som påføres på ulike deler av kroppen varierer fra 0 til 1,2 mg/cm^2. Et stort antall av personer som soler seg opplever å bli solbrent. Dette kan delvis skyldes ubeskyttet soleksponering og delvis forskjeller i tykkelsen av solkrem påført på ulike deler av kroppen.

4. Er det nødvendig med spesifikke grenseverdier for solbeskyttelsesfaktorer mot UV-stråling? Er det nødvendig å angi separate verdier for beskyttelsesfaktorer for UVB- og UVA-stråling? Gi en logisk begrunnelse for de foreslåtte verdiene.
Så sent som i 2006 viste en norsk undersøkelse av 15 ulike solkremer at 3 av produktene (20%) ga svært svak eller ingen beskyttelse mot UVA-stråling. Seks av de testede produktene (40%) holdt ikke mål i forhold til EU-kommisjonens nye anbefalinger om solkremers evne til å beskytte mot UV-stråling. Disse resultatene illustrerer tydelig behovet for en strengere regulering av solkremmarkedet. Numerisk angivelse av solfaktor på solkremer bør avvikles ettersom den ofte kan medføre mer forvirring enn klarhet. Produktene burde heller ha en kvalitativ merking som fokuserer på beskyttelsen. Solkremer bør ha en merking som angir lav, middels, høy eller veldig høy beskyttelse. Det er viktig å gjøre befolkningen oppmerksom på mulige alvorlige helseeffekter som kan forårsakes av soling. Voksne som blir eksponert for sterkt sollys (UV-indeks ≥ 4) bør oppfordres til å bruke solkremer med høy eller veldig høy beskyttelse. Foreldre bør oppfordres til å sørge for at barna deres bruker solkrem med høy eller veldig høy beskyttelse under forhold hvor UV-indeks ≥ 3. Produkter med en solfaktor for UVB-beskyttelse lavere enn 6 bør ikke klassifiseres som solkrem ettersom de ikke gir noen praktisk beskyttelse. Når det gjelder UVA-beskyttelse, anbefaler Europarådet og de nye anbefalingene fra EU-kommisjonen at forholdet mellom PPD/SPF ≥ 1/3. Verdien av den kritiske bølgelengden skal være over 370 nm for at en solkrem kan sies å ha bredspektret beskyttelse.

ANBEFALINGER

1. *Solbeskyttelsesfaktoren (SPF) fastsatt in vivo (Colipa 2006) bør benyttes som indikator for UVB-beskyttelse.*
2. *"Persistent pigment darkening"(PPD) fastsatt in vivo bør benyttes som indikator for UVA-beskyttelse.*

3. *"Persistent pigment darkening"(PPD) fastsatt in vivo bør videreutvikles med formål om å oppnå internasjonal enighet om metoden og analyseprosedyrene.*
4. *Betegnelsen "solbeskyttelsesmidler" og tilsvarende betegnelser indikerer at produktet beskytter både mot UVB- og UVA-stråling. Beskyttelsen mot UVB skal være i overensstemmelse med en SPF ≥ 6. Beskyttelsen mot UVA skal være i overensstemmelse med at forholdet mellom PPD/SPF ≥ 1/3 og at verdien av den kritiske bølgelengden er over 370 nm.*
5. *Følgende betegnelser bør brukes for å angi beskyttelse mot erytem: Lav beskyttelse (6,0 ≤ SPF ≤ 14,9); Middels beskyttelse (15,0 ≤ SPF ≤ 29,9); Høy beskyttelse (30,0 ≤ SPF ≤ 59,9); Veldig høy beskyttelse (60,0 ≤ SPF).*
6. *Det er nødvendig med flere studier for å nærmere kunne avklare forholdet mellom tykkelse av påført solkrem og solbeskyttelse.*
7. *Det er ønskelig å utvikle internasjonalt harmoniserte in vitro-metoder for måling av et produkts solbeskyttelse.*

ACKNOWLEDGEMENTS

The Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) has appointed an *ad hoc* group consisting of both VKM members and external experts to answer the request from the Norwegian Food Safety Authority. The report from the *ad hoc* group has been discussed and approved by the VKM's Scientific Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics.

Ad hoc group:
The members of the *ad hoc* group are acknowledged for their valuable contribution to this opinion.

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Persons working for VKM, either as appointed members of the Committee or as *ad hoc* experts, do this by virtue of their scientific expertise, not as representatives for his/her employers. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

The opinion has also been submitted for consultation among relevant expertise in the Norwegian Cancer Society, Cancer Registry of Norway, Norwegian Dermatological Society, Norwegian Institute for Air Research, Norwegian Pollution Control Authority and the National Council of Nutrition.

VKM wishes to acknowledge Dr. Ola Engelsen at the Norwegian Institute for Air Research for providing figure 9 on solar exposure and vitamin D production and Senior Scientist Bjørn Johnsen from the Norwegian Radiation Protection Authority for his contribution to figure 1 and 2 related to the irradiance and spectrum of solar radiation and the global UV-index at different latitudes in this opinion.

Assessed by:

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1. BACKGROUND

The European Commission has recently established recommendations to make sure that sunscreen products manufactured and sold on the European market should provide for a minimum degree of protection against UVB- and UVA-radiation. The recommendations are given in "Commission recommendation of 22 September 2006 on the efficacy of sunscreens products and the claims made relating thereto" (EC, 2006[1]), and they are mainly based on a resolution (ResAP(2005)4) from the Council of Europe, Committee of Ministers on sun protection products to optimise consumer protection (COE, 2005[2]). The resolution from the Council of Europe refers to recommendations from the American Academy of Dermatology (AAD) and investigations carried out by the French health agency *Agence francaise de securite sanitaire des produits de sante* (AFSSAPS).

It is stated in the recommendations from the European Commission that sunscreen products should be sufficiently effective and provide a minimum protection against both UVB and UVA-radiation to ensure a high protection of public health. This implies that the protection against UVB- and UVA-radiation should be related and an increased sun protection factor (SPF) (i.e. mainly UVB protection) should include an increase in the UVA protection as well. Scientific findings have shown that certain biological damage to the skin can be prevented and reduced if the ratio of the protection factor measured in the persistent pigment darkening (PPD) test (i.e. addressing mainly UVA-radiation) is at least 1/3 of the factor measured by the SPF testing method. Moreover, in order to ensure a broad protection, the value of the critical wavelength should exceed 370 nm[1,2].

In order to reach the protection level indicated by the SPF, sunscreen products have to be applied in quantities similar to the ones used for testing, i.e. 2 mg/cm^2, which equals approximately 36 grams (or 6 teaspoons of lotion) for the body of an average adult person. As this quantity is higher than what is usually applied by the consumers, the instructions of a sunscreen product should state the quantity of the product which has to be applied to reach the declared SPF. Accordingly, sunscreen products should be labelled with "if the recommended quantity applied is reduced by half, protection may fall by as much as two-thirds"[1,2].

In 2006, the National Veterinary Institute (Veterinærinstituttet) and the Norwegian Food Safety Authority (Mattilsynet) carried out a survey where the protection against UVA-radiation provided by 15 sunscreens sold on the Norwegian market was measured. The results showed that 3 of the sunscreens did not follow the recommendations for UVA protection from the European Commission, and their ability to protect against UVA were poor or absent. The declaration on 2 of these 3 products claimed that the sunscreens protected against both UVA and UVB-radiation[3].

The Norwegian Food Safety Authority would like to have an inclusion of these new recommendations for sunscreen products in the Council Directive of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (76/768/EEC).

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[1]EU Commission Recommendation of 33 September 2006 on the efficacy of sunscreen products and the claims made relating thereto. Off J European Union. 26.9.2006.

[2] Council of Europe, Committee of Ministers. Resolution ResAP(2005)4 on sun protection products to optimize consumer protection. (Adopted by the Committee of Ministers on 1 December 2005 at the 949th meeting of the Ministers' Deputies).

[3]National Veterinary Institute. Kontroll av UVA – beskyttelse i 15 utvalgte solkremer, 2006-14-26, June 2006 (in Norwegian).

They have therefore asked for a risk assessment from the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) on possible health effects which could be related to not applying a sufficient quantity of the sunscreen product to reach the declared SPF, or by using sunscreen products with an insufficient UVA protection.

2. TERMS OF REFERENCE

The Panel on Food Additives, Flavourings, Processing Aids, Materials in contact with Food and Cosmetics is requested to answer the following questions in relation to the solar radiation and use of sun protection products.

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

2. *What are the specific health and safety implications (negative and positive) relating to the use of sun protection products during exposure of persons to solar radiation?*

3. *When and where are sun protection products used? How much and what type of sunscreen products are used?*

4. *Are specific limit values of sunscreen protection factors to solar radiation necessary? Is it necessary to give different values for the protection factors of UVB and UVA? Give the rational for the proposed values.*

3. OPINION

3.0. Introduction

The purpose of sunbathing is to achieve a tan. Many people claim that sunbathing makes them feel good. Tanning represents currently a socially desirable appearance. Tanning is primarily a defense mechanism that opposes to the penetration of UVR. The accompanying thickening of the epidermis participates greatly to this defense and to a lesser degree to the stimulation of the pigmentary defence system. Moreover, adequate exposure to solar radiation has also an important role in human health through UV-induced production of vitamin D.

Nuclear reactions in the inner of the sun lead to production of large amounts of energy, which are transported out of the sun by radiation from the surface. The dominating radiation emitted by the sun is in the optical region of the electromagnetic spectrum. The radiation contains photons in the wavelength range between approximately 190 nm and several thousand nm with a maximum emission in the green part of the visible spectrum. The electromagnetic spectrum is shown in Fig. 1. Infrared, visible and ultraviolet (UV) radiation is termed optical radiation and UV is further subdivided as indicated. The solar spectrum contains UVB, UVA, visible, and infrared radiation when it reaches the surface of the earth.

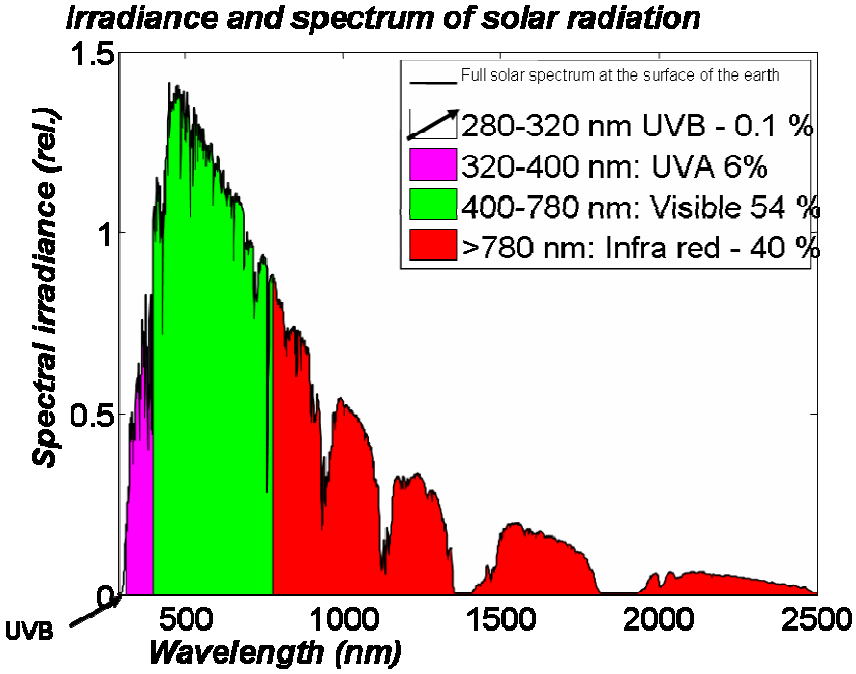


Fig. 1. *The global spectral irradiance spectrum [W/m^2/nm] at summer noon, 60^{o}N[4]. The photon energy is proportional to the frequency of the radiation and inversely proportional to the wavelength (E=hν = hc/λ). (from B. Johnsen, NRPA, based on Mayer and Kylling (2005))*

[4]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 (315-400 nm); a barium-flint-pyrex filter defined the UVB (280-315 nm); and a pyrex filter defined the UVC (wavelengths shorter than 280 nm). So the basis of these divisions has its grounding in physics, and not biology, although these definitions have been very useful in biology. The above definitions 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 (320-400 nm), UVB (280-320 nm) and UVC (190-280 nm).

Due to interaction processes in the atmosphere, the spectrum and intensity of the radiation is modified before the radiation reaches the surface of the earth. Ozone in the atmosphere absorbs all UVC-radiation and a considerable portion of the UVB-radiation. Variations in the effective thickness of the ozone layer are a major cause of seasonal, geographical, and temporal variations in the local UV-dose.

The amount of radiation absorbed or scattered increases exponentially with the effective thickness of the atmosphere. The sun elevation is expressed as the solar zenith angle (SZA) that is the angle between a vertical line and a line towards the sun. Thus, the angel is zero when the sun is in zenith (i.e. straight above our heads). SZA determines the dose reaching the earth given that the atmospheric conditions are constant. The effective thickness (path length of sun rays) then is the thickness of the atmosphere in the direction of zenith times the cosine of the SZA. Due to the dominating role of scatter in air molecules and absorption in the ozone layer, radiation with the shortest wavelengths are reduced more by increasing SZA than radiation with longer wavelengths. Therefore, the sun looks red at sunset. SZA varies regularly with time of day and season and the latitude determines the range of these variations. This regular variation in the solar SZA also determines the ratio between UVA and UVB reaching the surface of the earth. At low SZA, the relative amount of UVB will be large, implicating much UVB in the middle of the day and near equator. Similarly, the solar spectrum in early morning or late afternoon and at high latitudes is almost free from UVB. UVA is less affected by SZA.

The internationally agreed UV-index (UVI) scale is defined in terms of the erythemally weighted irradiance (i.e. the intensity contributing to skin reddening). (See WHO http://www.who.int/uv/intersunprogramme/activities/uv_index/en/index.html). It is a simple tool to be used for information purposes towards the general public to indicate level of photo protection needed for a given location and time. Daily publication of this index in newspapers and electronic media is of great benefit for safe sun behaviour.

It should be emphasised that UV-index is strongly weighted to UVB and does not give information about the risk of other biological endpoints than erythema. To give an idea of the meaning of the UV-index, it may roughly be assumed that a fair skinned person without previous UV exposure will develop a slight reddening in about ½ hour in sunshine with UV-index 5. Under conditions where the UV-index is 10, the reddening will occur in ¼ hour because the UV-index is linear. Several institutions offer updated values and forecasts of UV-index for larger or smaller areas. For Europe, the mid-summer, midday, clear sky UV-index varies from about 10 in the south to 5 in the north. UV-index = $40 \int I(\lambda)\, w(\lambda) d\lambda$, where $I(\lambda)$ is the irradiance on a horizontal surface expressed in W/m^2, $w(\lambda)$ the erythemal weighting function and the arbitrary constant 40 has the unit m^2/W and was chosen to give practical and informative numerical values. UV-index is unitless.

A number of global and local factors will influence the UV irradiance used to calculate UV-index.

- Depletion of the ozone layer has been observed over the last decennia. At northern mid-latitudes, the reductions have been maximally 7% on a yearly basis. Due to the international agreement to reduce the emission of ozone depleting substances, the Montreal protocol, the ozone layer will probably recover in 50-100 years. Local day-

to-day variations are frequently observed due to meteorological factors. These variations have been shown to be as large as 40%.

- Thin clouds may transmit more than 90% of the UV radiation. Under particular atmospheric conditions, clouds may even increase UV-index due to scatter of radiation. More heavy cloudiness will reduce UV-index to almost zero.

- Surface reflection and scatter, albedo, is dependent on the surface cover, whether it is composed of reflecting material like snow or absorbing, dark substances. The albedo can have values between 90 and 0%, and white snow may increase the UV-index by 80%. Snow-cover (in mountains) will increase the UV-index at sites up to several km away from the snow-covered areas.

- Altitude increases UV-index due to several factors; the effect of atmospheric absorption and scatter is reduced and the horizon is wider, i.e. more free sky is visible. The sky transmits scattered radiation to the surface. Normally the effect of latitude is in the order of 5 - 10% increase in UV-index per 1000 m increases in altitude.

- Aerosols have marked effects on solar radiation through scatter. In addition, absorption in gases in the troposphere reduces UV-index. These effects are mostly caused by pollution and can be readily observed near big cities. In extreme cases, UV-index can be reduced by 5 units in mid summer in the tropics, but a more typical figure is 20%.

- UV-index is defined on the basis of irradiance on a horizontal surface, but in order to assay the biological influence of the radiation, measurement of actinic flux will be more representative. Biological action is independent on the direction of the radiation. Therefore, the effect on the skin is larger on areas directed directly towards the sun. Physical measurements including radiation in all directions or chemical actiniometers may be used to determine the actinic flux. Such measurements are largely unavailable at most locations.

Examples of the changes in UV-index during the year in cities at different latitudes in Europe are shown in Fig. 2, while Fig. 3 gives an example of the changes in UV-index in Oslo (60^{o}N) during a summer day and the concurrent intergraded Standard Erythema Dose (SED; see page 16).

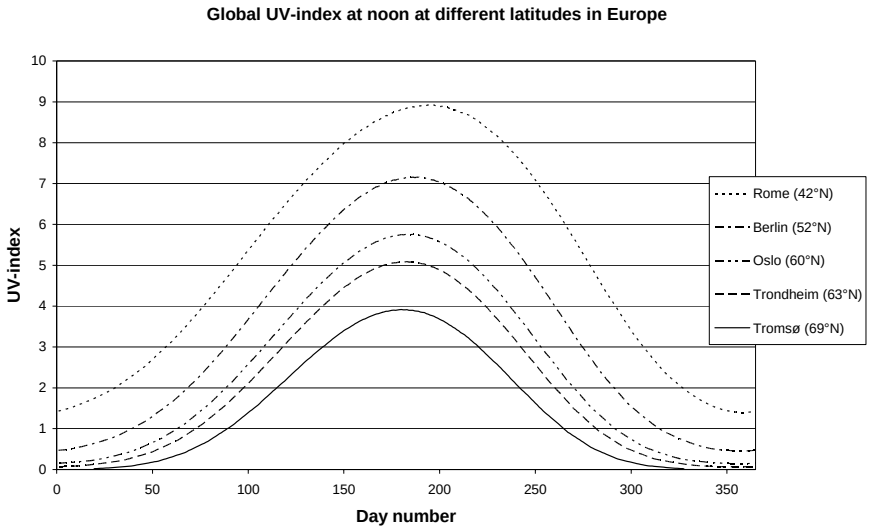
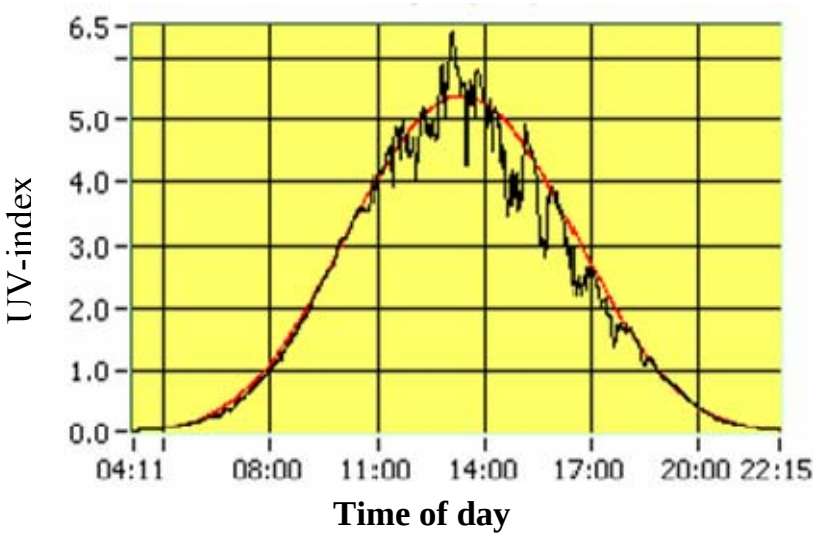


Fig. 2. *Calculated noon UV-indices at different latitudes in Europe on each day of the year, starting on 1 January. In the calculations clear sky, typical thickness of the ozone layer and a 5% reflection from the ground have been assumed (from Bjørn Johnsen, NRPA, based on Mayer and Kylling (2005))*



Time of day	UV-index (mean)	SED (integrated)
09 – 11	2.9	4.8
11 – 14	5.1	12.9
14 – 17	3.7	9.7
Sum dose		27.4
Max intensity	6.4	

Fig. 3. *The UV-index, measured (black curve vs. averaged value in red) 5th July 2006 in Oslo, and calculated doses during the full day and in given time intervals. Maximum sun elevation for the day = 52.6 degrees (http://www.nrpa.no/uvnett).*

Penetration of UV-radiation in the skin is strongly dependent on the wavelength and the colour of the skin. Melanin is an efficient absorber of UV-radiation and the structure of the skin scatters the radiation in all directions as it enters the tissue. UVB penetrates down to only a few micrometers (μm) while a certain amount of UVA can go through the epidermis and irradiate underlying tissues, e.g. the blood vessels (Fig. 4).

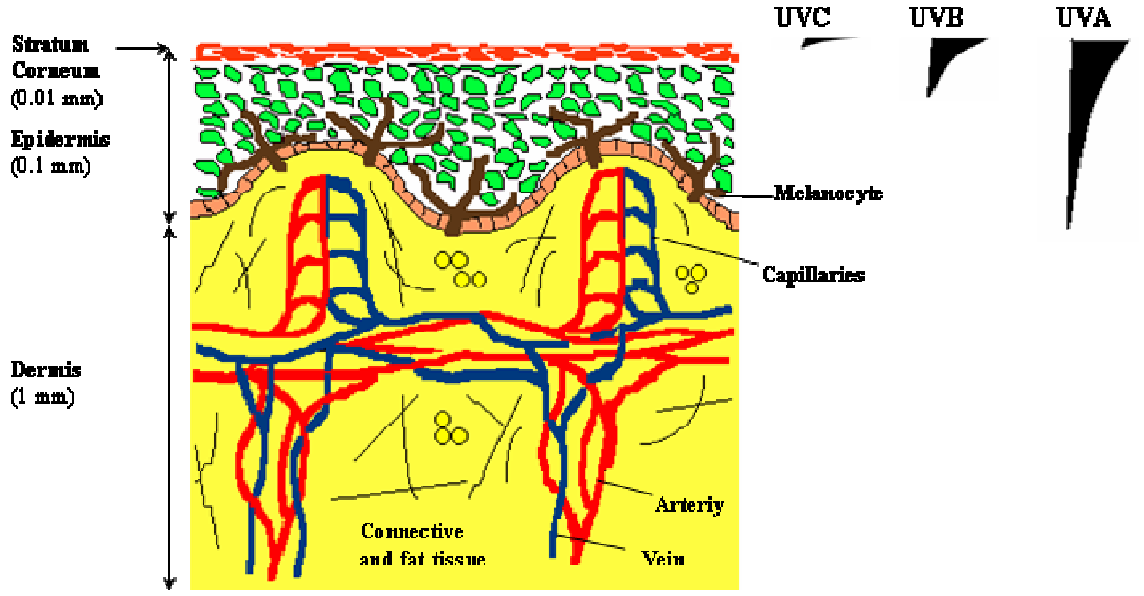


Fig. 4. *Penetration of UV-radiation through the skin. On the left a simplified skin model is shown. The exponential decrease in light dose (fluence; i.e. the dose received by a cell in the tissue) is illustrated on the right. The expression "penetration depth" is commonly used and defines a level where 37% of the radiation energy is left. Due to the nature of the attenuation of radiation, approximately 10% of the energy is left after two penetration depths and a tiny fraction of the radiation will penetrate a large number of penetration depths. (Bredholt, Nilsen and Christensen, personal communication)*

UVA comprises more than 90% of terrestrial UV-radiation, and penetrates into the dermis, whereas the shorter UVB wavelengths, are up to a thousand times more effective in producing sunburn, but penetrate primarily the more superficial epidermis. UVB is associated primarily with direct effects on cellular DNA, while UVA is associated with indirect damage to the cells through production of free radicals.

Questions similar to the four questions raised in the Term of References have also been addressed by Council of Europe (2005) and EU Commission Recommendation (2006). The response to the first question is to a large extent based on the EU Scientific Committee on Consumer Products Opinion on biological effects of ultraviolet radiation relevant to health with particular reference to sunbeds for cosmetic purposes (SCCP, 2006a).

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

3.1.1. Negative Effects
3.1.1.1 Acute

Skin
Exposure of the skin to solar UVR results in inflammation (erythema/sunburn) that appears a few hours after exposure and culminates between 24 and 36 hours, then disappears on the 3rd day, to be replaced by pigment darkening in melano-competent persons (not skin type I and albinos). This response is primarily induced by its UVB component. UVA can also cause erythema but at much higher doses (Kagetsu *et al.,* 1985). It is assumed that UVA contributes to about 15 – 20% of sunburn from solar radiation (IARC, 2001).

Solar erythema 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 known as sunburn cells (Sheehan and Young, 2002). The sunburn can involve tenderness, pain, swelling, and blistering and may be accompanied by fever, headache, and vomiting, depending on the size of the damaged areas and the dose received.

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 MED
I	High	None	Melano-compromised	1 – 3
II	High	Poor		
III	Moderate	Median	Melano-competent	3 – 7
IV	Low	Dark		
V	Very low	Natural brown	Melano-protected	7 - >12
VI	Extremely low	Natural black		

Individual sensitivity to erythema can be assessed by determining the minimal erythema dose (MED) that increases with skin type as shown in Table 1 (Harrison and Young, 2002). The unit of erythemal radiation is the Standard Erythema Dose (SED), where 1 SED is equivalent to an erythemal effective radiant exposure of 100 J/m^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 painful, blistering sunburn. In the British population, about 11%, 30%, and 31% of people are of skin types I, II and III, respectively.

Within a few days after exposure to solar UVR, delayed melanogenesis (tanning) occurs that is dependent on skin type and like erythema is primarily caused by UVB. Tanning results from the synthesis of melanin in melanocytes: specialized pigment producing cells in the epidermis that transfer melanin to keratinocytes. As a reaction to aggression by UVB-radiation, the keratinocytes of the basal layer actively divide on about the 3rd day, thus

contributing to global thickening of the epidermis. The Malpighian layer will double in thickness, and the number of layers of the stratum corneum will also increase. In the absence of further irradiation, peeling causes the thickened epidermis to return gradually to normal (in 5 weeks). In the case of a single exposure, the tan persists for 3 – 4 weeks. 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. Tanning cannot be viewed as a beneficial health effect of exposure to solar radiation. The UVB tan results in a modest photoprotection against erythema equivalent to a sunscreen with a sun protection factor (SPF) of 2 – 3 (Agar and Young, 2005). A certain degree of photoprotection is therefore obtained, the extent of which also depends on the neo-melanins synthesized (see below).

Solar radiation may induce polymorphic light reaction (PLE), commonly known as solar eczema in as much as 10-15% of the Nordic populations, commonly seen at springtime, as an highly itching eczema in UV exposed areas such as face, upper chest and arms. PLE may be induced by both UVA and UVB.

The pigment darkening induced by UVA-radiation is a result of oxidation of melanin and its precursors and is seen shortly after exposure. It is called immediate pigment darkening (IPD). This skin pigment darkening is temporary. When exposure ends, the color fades rapidly for two hours, and then more slowly for 24 hours. A melano-compromised person does not develop this reaction. The tans primarily induced by UVA are not photoprotective against erythema (Gange *et al.,* 1985). UVA-radiation, which is only slightly absorbed by the epidermis, does not lead to thickening of the skin, and therefore hardly causes any peeling.

The presence in the integument of endogenous substances (porphyria) or exogenous substances (medicines) can trigger phototoxic effects which present clinically as severe sunburn. Phototoxic reactions are restricted to exposure and substance deposit sites in cases where short lived photoproducts e.g. singlet oxygen or hydroxyl radicals are induced. Longer lived photoproducts may in rare cases diffuse a certain distance before they exert their effects. Examples of long lived photoproducts from endogenous substances are the UV photoproduct of urocanic acid, cis-urocanic acid, and the photoisomers of bilirubin formed during phototherapy. Some drugs (e.g. NSAIDs) may also be metabolised under influence of UV-radiation to photoproducts with toxic or phototoxic potential (Western *et al.,* 1987, Encinas *et al.,* 1998).

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*,* 1999). Photoalleric reactions, often eczematous, extend far beyond the exposed areas. They require prior contact with the allergen.

The skin's immune defenses protect against external aggression (bacteria, fungi, and viruses). UVR induces local as well as systemic immune suppression at skin sites distant from that which was irradiated. The immune defenses are considerably impaired even by weak doses of solar radiation (below the erythemal dose). This depression is reversible, and its restoration takes around 3 weeks. Suppression of cell-mediated immunity is thought to play a role in infectious diseases, e.g. Herpes simplex infections and possibly also in induction of skin cancer. The effects of UVR include depletion from the skin of Langerhans cells, epidermal

dendritic antigen-presenting cells, which pick up antigen and transport it to local lymph nodes where they activate specific T lymphocytes. UVR also disrupts production of cytokines by various cells in the skin, creating an environment which is not conductive to activation of immunity. 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 (Nicole *et al.,* 2005).

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; Agar *et al.,* 2004). 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.

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, except in younger persons where a certain amount of UVA will penetrate to the level of the retina (Sliney, 2001; Roberts, 2001; Johnson, 2004).

The most common acute clinical effect of UVR on the eye is photokeratitis, also known as snow blindness or welder's flash (Sliney, 2001; Roberts, 2001; Johnson, 2004). This is a painful transient inflammatory condition caused by 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.

"Blue light" photochemical retinal damage can occur under influence of intense exposure in the wavelength region from 300 to 700 nm (ICNIRP 1999). Visual pigments as well as other chromophores are believed to be involved in the complex reactions leading to this radiation effect. The injury may take place during acute episodes of viewing the sun at eclipse with inadequate filters. It has also been assumed that the condition may occur as a result of prolonged exposure over years. Furthermore several authors have hypothesized that photochemical damage may be a part of the ethiology of age–related macular degeneration (AMD) (Ham *et al.*, 1976; Boulton *et al.,* 2001; Akyol *et al.*, 2002).

3.1.1.2 Chronic

Photoageing

The changes seen in human skin with age are due to a combination of ageing of the skin *per se* and ageing of the skin due to exposure to sunlight (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. Ageing skin is

characterized primarily by atrophy (Gilchrest *et al.,* 1996). Ageing results in a thinner, more transparent skin, increasing prominence of the underlying vasculature and loss of elasticity. While there are relatively few changes in the stratum corneum, the epidermis thins and the rete ridges are affected, reflected histologically by flattening of the undulations of the dermo-epidermal junction. The dermis also thins with age, resulting in more fragile skin.

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).

Actinic keratoses

The pathology of actinic keratoses (AK) if biopsied, shows epidermal dysregulation, and loss of the normal maturation pattern of epidermal keratinocytes, but no invasion of these keratinocytes into the underlying dermis. AK arise on visibly sun-damaged skin which is dry, wrinkled, and may exhibit pigmentary irregularities. The lesions are most commonly seen on the face, the scalp in males, and the backs of the hands in both sexes. They are seen as raised scaling lesions which may ooze or crust and on the male face are easily traumatised while shaving (Salasche, 2002).

AK lesions are extremely common on white skin in exposed body sites after the age of 50 years in Europe and even earlier in sunnier climates such as in Australia. They are usually multiple, and are facultative precursors to squamous cell carcinoma (SCC) of the skin. The likelihood of an AK transforming to SCC is significant. Hence, an argument for treating AK is that this will prevent future SCCs. AK, if not treated, may persist, may involute spontaneously if protected from further UV radiation, or may progress to SCC.

Skin Cancer

An IARC (1992) monograph on solar and ultraviolet radiation classified solar radiation as "carcinogenic" to humans (Group 1). Basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma are the most important cancers due to solar radiation. 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).

Non-melanoma

The evidence for UVR in development of BCC and SCC has been primarily ecologic (reviewed by Armstrong and Kricker, 2001), supported by mouse studies in the case of SCC (de Gruijl, 1995). The role for UVR is supported by the presence of UVR "signature mutations" in tumors (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). An Australian study has recently shown that BCC of the trunk is associated with excessive sun exposure (Neale *et al.,* 2007). BCC and SCC result in a high level of morbidity with only occasional mortality from infrequent metastatic SCC. Many cancer registers do not record BCC and SCC.

BCC is the most common form of cancer and the least aggressive. Basal cells are cells that line the deepest layer of the epidermis. BCC is around four times more frequent than SCC. The risk of BCC increases with recreational exposure during childhood and adolescence, and the more sensitive an individual is to the sun, the higher the risk will be. The epidemiological evidence indicating a relationship between BCC and sun exposure suggests that short burning intermittent episodes of sun exposure are more important than chronic total cumulative lifetime sun exposure. BCCs are found mainly on the face in European populations, but also on other body sites such as the back. On the face they have a predilection for the central panel and are often found around the inner canthus of the eye, the sides of the nose and the forehead. There are different clincal variants of basalioma. The most common presentation is the nodular, slow growing lesion. Initially they are raised translucent domed lesions which slowly expand and eventually develop central ulceration. Superficial spreading basalioma are predominantly found on the trunk and can be hard to differentiate from e.g. solar keratosis or dermatitis, they grow horizontally, and may also be locally multifocal. Morpheaform or desmoplastic or sclerosing basaliomas are the clinically most aggressive forms, as they infiltrate into the deep dermal collagen, and can be hard to detect due to benign clinical expression. There are also rare forms of pigmented basalioma. All the basaliomas lack the capacity to metastasise, but can be very invasive locally, destroying cartilage and even bone.

A dozen case-control studies and at least three cohort studies in the USA and Australia have shown that there is a cumulative relationship between sun exposure and the risk of SCC cancer. SCC occurs on existing actinic keratoses (AK) that may be regarded as precancerous lesions for SCC. It is generally assumed that induction of SCC is due to UVB and that the action spectrum for induction of SCC is roughly similar to the action spectra for induction of erythema. A standard action spectrum has been published (CIE, 2006). UV-induced SCCs develop on visibly sun-damaged skin and are raised scaling nodules which may bleed. By comparison with AK, they have more depth on palpation but clinical differentiation between a large AK and an early SCC can be difficult, as can the pathological differentiation between these two entities.

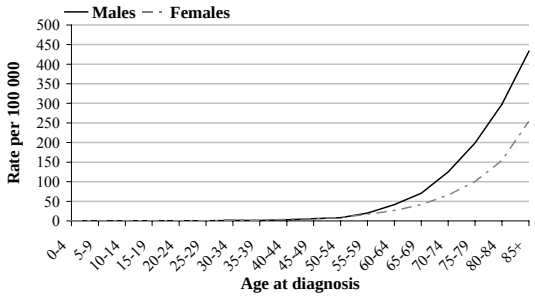


Fig. 5. *Age-specific incidence rates of SCC risks 2000 – 2005*. (Cancer Registry of Norway, 2006a; http://www.kreftregisteret.no)

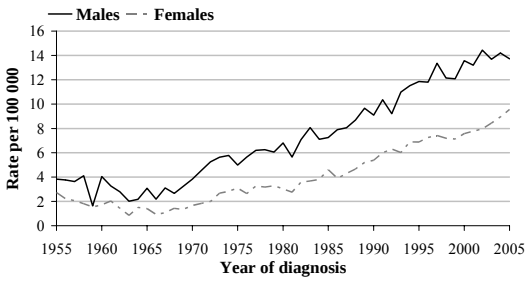


Fig 6. *Age-adjusted incidence rates of SCC risks 1953 – 2005*. (Cancer Registry of Norway, 2006a; http://www.kreftregisteret.no)

It is apparent from Fig. 5 that SCC in Norway occurs mainly after the age of 60 years. The shape of the curve is in agreement with other findings that the risk of SCC increases with the cumulative exposure to UVR. Fig. 6 shows that the age-adjusted incidence of SCC in Norway has increased nearly linearly both in males and females from about 1965 and it is expected that the number of SCC in Norway will increase with about 50% during the next 15 years (Cancer Registry of Norway, 2006b). In Europe, it is estimated that although the population of EU (25 member states) will remain constant between 2000 and 2015, a 22% increase in non-melanoma skin cancer in persons aged over 65, and 50% in those aged over 80, is to be expected (Boyle *et al.,* 2003).

Melanoma

Though 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).

Skin color and sun exposure are potent determinants of risk of melanoma. World incidence figures show that the risk to individuals is greatest where pale skinned people live at low latitudes such as Australia and New Zealand (Parkin *et al.,* 2003; Bulliard, 2000). In areas of the world where dark and pale skinned people 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 color and latitude as the peak incidence is in the north, in countries such as Norway and Sweden, where fair skinned people live an outdoor life and have access to sunny holidays in the south, or Switzerland where fair skinned people live at high altitude (Parkin *et al.,* 2003). Further evidence of 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).

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. The overall conclusions were that skin type I (versus IV) was associated with a relative risk (RR) of 2.1 (95% confidence interval 1.7-2.6) for melanoma. A high density of freckles was associated with a RR=2.1 (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). Risk of melanoma is also greater in persons with larger numbers of melanocytic naevi. Numerous case-control studies have addressed the influence of naevi, and a second meta-analysis by Gandini and co-workers (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 (RR = 6.9, 4.6-10.3) as was the number of atypical naevi (RR = 6.4, 3.8-10.3; for 5 versus 0). Twin studies have provided strong evidence that naevus number is genetically determined (Wachsmuth *et al.,* 2001) 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. 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 (1.4-2.9). A similar study from the Swedish Cancer Registry estimated the standardized incidence ratio for melanoma to be 2.4 (2.1-2.7) for offspring if one parent had a melanoma, 3.0 (2.5-3.5) for an affected sibling and 8.9 (4.3-15.3) if a parent and a sibling were both affected. The highest ratio was 61.8 (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.

A third meta-analysis reported by Gandini and co-workers (2005c) has supported the conclusions of many individual case-control studies that intermittent sun exposure remains the most predictive environmental risk factor for melanoma (RR=1.6, 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, 1.7-2.4). The pooled analysis provided no evidence for a causal effect of chronic sun exposure on melanoma risk, RR=1.0 (0.9-1.0).

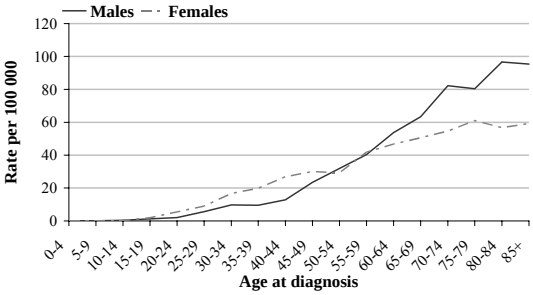


Fig. 7. *Age-specific incidence rates of melanoma risks 2000 – 2005*. (Cancer Registry of Norway, 2006 a; http://www.kreftregisteret.no)

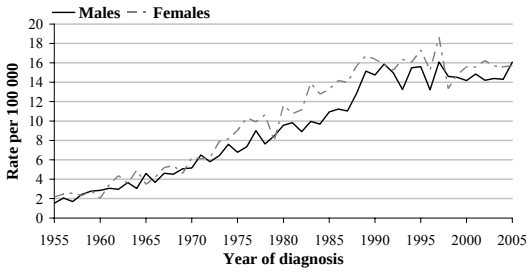


Fig 8. *Age-adjusted incidence rates of melanoma risks 1953 – 2005*. (Cancer Registry of Norway, 2006 a; http://www.kreftregisteret.no)

It is apparent from Fig. 7 that the risk of melanoma in Norway starts to increase already at the age of 20 year. Thus, the shape of the curve is very different from that of SCC where the risk increases with the cumulative exposure to UVR. Fig. 8 shows that the age-adjusted incidence of melanoma in Norway has increased nearly linearly both in males and females from about 1965 and that it has been nearly constant from about 1995. However, in men older than 50 years an increase is observed. It is expected that the age-adjusted incidence will decrease slightly during the next 15 years (Cancer Registry in Norway, 2006b), while there is evidence that the incidence rate in Europe is increasing substantially (Boyle *et al.,* 2004).

In summary, there is strong evidence that excessive sun exposure is causal for most melanomas. 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.

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 odds ratio (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.

3.1.2 Positive Effects

Vitamin D

There is a broad consensus that a lack of adequate vitamin D is a serious health issue. Evidence of causality is compelling for some bone and muscle disorders and particularly for osteoporosis and resultant fracture. There is some evidence from individual epidemiological studies, and from ecological studies, of an increased risk of autoimmune diseases, including multiple sclerosis, type-1 diabetes and rheumatoid arthritis with low vitamin D status. However, the strength of this evidence is, as yet, insufficient to establish a causal association and should be the subject of further research. At present, there is limited evidence for a possible association with prostate, breast and other cancers but somewhat stronger evidence of an association with colon cancer.

Two forms of vitamin D exist, vitamin D2 (ergocalciferol) and D3 (cholecalciferol). Vitamin D2 is produced by UVB irradiation of ergosterol which is present in yeast and fungus. Vitamin D3 occurs in seafood and is formed in humans by solar radiation. It has probably a higher biological activity than D2.

The sun is the most important source for the formation of vitamin D in the body. When the skin is exposed to UVB provitamin D (7-dehydrocholesterol) is converted to pre-vitamin D3 by a photolytic conversion. Vitamin D3 is subsequently formed by thermal isomerization. Inactive metabolites are formed with long-lasting exposure thereby vitamin D will not reach toxic levels following sun exposure. The first step in the metabolic activation of vitamin D is hydroxylation of carbon 25 with formation of 25-hydroxyvitamin D3 (25(OH)D) which occurs primarily in the liver. The second step is the formation of 1α25-dihydoxyvitamin D (1,25-(OH)2D). 25(OH)D is the most important metabolite and have a half life of 3 – 4 weeks. The concentration of 25(OH)D reflects how much vitamin D that is available and is used as a measure of vitamin D status.

The production of vitamin D in the skin is dependent on many factors such as pigmentation, age, use of sunscreen, season of the year, latitude, surface reflection, thickness of the ozone layer and weather. The ability of the skin to produce vitamin D is reduced at increasing age. At the same UVB exposure a person 70 years old will only produce 25% of the amount of vitamin D as a person 20 years old. Moreover, afro-American individuals will need about 7 times longer exposure than a north-European with sun-sensitive skin to produce the same amounts of vitamin D by sun exposure. Vitamin D will only be formed in the skin when the UVB intensity is above a certain level. At latitude above 35^{o}N, for example Rome (42^{o}N), Paris (48^{o}N), London (51^{o}N), and Oslo (60^{o}N) winter sunlight during part of the day lacks UVB and is incapable of producing vitamin D. Fig. 9 shows the number of hours per day with sufficient UVB-radiation for vitamin D production in the skin. The daily period of vitamin D production varies with time of the year and latitude. Thus the "vitamin D winter" last from November to the middle of February in Oslo (60^{o}N) and from the middle of October to March in Tromsø (70^{o}N) (Directorate of Health and Social Affairs, 2006).

It has been reported that exposure of the whole body to a MED-dose corresponds to an intake of about 250 μg Vitamin D. From these results it has been estimated that at noon in June in Boston (42^{o}N) 5 – 15 minutes sun exposure to the face and backs of hands (5% of total body surface) 2 – 3 times a week is sufficient to cover the vitamin D requirement.

The question of what an "optimal" level of vitamin D nutrition status might be is equivalent to asking what the optimal concentration of 25(OH)D in plasma or serum is for the overall health of humans. The question is difficult to answer at present because there is still much to be learned about the relationship between 25(OH)D and human health. Several participants at a recent workshop (McKinlay, 2006) favoured a level of 75 nmol/l as being a minimum acceptable level particularly in relation to reducing the risk of osteoporosis. This would be the case for some older adults, however, there is still much uncertainty about optimal levels appropriate for other groups, for example young adults. It is of interest to note that many national authorities recommend daily intakes equivalent to much less than 75 nmol/l. In a recent Norwegian report from The National Council of Nutrition the following limits of 25-hydroxyvitamin D (25(OH)D) in serum were proposed: >50 nmol/l satisfactory, 25 – 50 nmol/d suboptimal, 12.5 – 25 nmol/l vitamin D deficiency, ≤ 12.5 nmol/l severe vitamin D deficiency. The Council recommended an intake of vitamin D of 7.5 μg/d from the age of 2 to 60 years old, and 10 μg/d for infants 6 – 23 months of age and persons older than 60 years (Directorate of Health and Social Affairs, 2006). The intake from food in Norway (fish oil and other food supplement excluded) during the last 25 years has been about 4 – 4.5 μg/d.

In Norwegians born and living in Oslo (60^{o}N), the great majority had 25(OH)D levels of 74.8 $\pm$ 23.7 nmol/l (varying from about 70 nmol/l during the winter to 80 nmol/l in the summer) (Meyer *et al.,* 2004). In a similar population from Tromsø (69^{o}N) the average 25(OH)D level was 62.1 $\pm$ 18.0 nmol/l (Jorde *et al.,* 2007). In general, the Norwegians seem to have a good vitamin D status compared to populations further south in Europe, probably due to vitamin D fortification of butter and margarine and a widespread use of cod liver oil, fat fish diet, and vitamin supplements. Although there is no general association between age and 25(OH)D levels among Norwegians, many elderly have a low vitamin D status due to their reduced vitamin D production in the skin and low physical capacity, which may cause too little sun exposure. Low vitamin D status is also seen among teenagers, mostly because of their low vitamin D intake. In Norway, immigrants from the non-Western world, particularly Pakistan, represent a high risk group of vitamin D deficiency, partly because of dark skin pigmentation and low vitamin D production and partly because of low vitamin D intake.

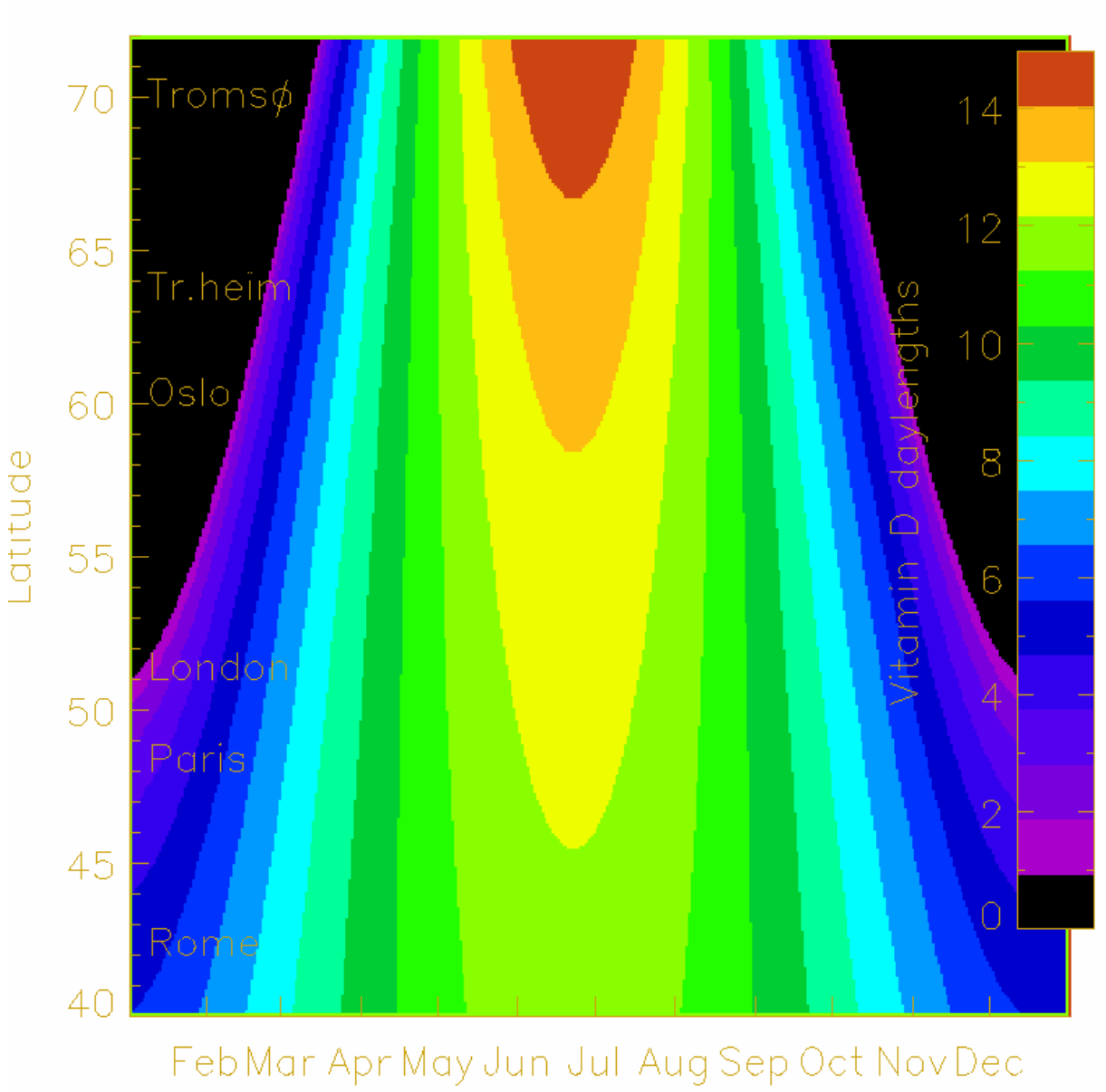


Fig. 9. *Number of hours per day (daily period) with sufficient UVB-radiation for vitamin D production in the skin. The daily period of vitamin D production (indicated with colour scale) varies with time of the year (x-axis) and latitude (y-axis). The calculation is based on the conditions of clear atmosphere, no surface reflection and a typical level of total ozone (300DU). (Ola Engelsen, NILU, personal communication)*

Feel good

The most common reason given for sunbathing is that the time in the sun brings a psychological feeling of well being and relaxation. The physical warmth of the sunrays also is very pleasant. After being tanned, most people feel better about themselves. 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.

3.1.3. Relative effects of UVB and UVA

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.

UVB is generally 3 to 4 orders of magnitude more effective per unit physical dose than UVA. 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). 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.,* 2003). By laser microdissection of human epidermal basal cells there has been found UVA-induced DNA damage. This implicates that UVA may be a more important carcinogenic factor than previously believed (Agar *et al.,* 2004).

Cyclobutane pyrimidine dimers, a typical UVB-induced DNA damage, were found to be produced in significant yield also in whole human skin exposed to UVA through a mechanism different from that triggered by UVB. Moreover, the latter class of photoproducts is produced in a larger amount than 8-oxo-7,8-dihydro-2-deoxyguanosine, the most common oxidatively generated lesion, in human skin. Strikingly, the rate of removal of UVA-generated cyclobutane pyrimidine dimers was lower than those produced by UVB irradiation of the skin. Finally, Mouret and coworkers (2006) compared the formation yields of DNA damage in whole skin with those determined in primary cultures of keratinocytes isolated from the same donors. It was found that human skin efficiently protects against UVB-induced DNA lesions, whereas very weak protection is afforded against UVA. These observations further emphasize the likely role played by the UVA-induced DNA damage in skin carcinogenesis and should have consequences for photoprotection strategies.

The action spectra of erythema (CIE 1998; Young *et al.,* 1998) are primarily in UVB. As pointed out earlier, UVA contributes only to about 15 – 20% of the weighted dose when a typical solar mid-day spectrum is multiplied with the relative spectral effectiveness. Delayed pigmentation (Parrish *et al.,* 1982), DNA photodamage (Young *et al.,* 1998) and photoisomerization of urocanic acid (McLoone *et al.,* 2005) are likewise primarily due to UVB. 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 immediate pigment darkening (IPD) shows that UVA is more effective than UVB (Irwin *et al.,* 1993). UVA has also been found to play an important role in photoaging (Yin *et al.,* 2003). Reactive oxygen species formed by interaction with UVA is assumed to be involved in photoaging (Krutmann, 2000). UVC is not an issue for terrestrial solar UVR because it is completely absorbed by the ozone layer.

The wavelength dependencies for SCC have been determined in hairless mouse models (de Gruijl, 1995; Kligman and Sayre, 1991) and these studies have shown action spectra essentially similar to that for human erythema (CIE, 1998, 2006; Young *et al.,* 1998). The

action spectrum for vitamin D formation (CIE 1998, 2000) is also similar to the action spectrum for erythema.

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 for skin cancer. 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 (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).

The wavelength dependency for melanoma has been discussed to a considerable extent since this represent the most serious cancer in relation to solar radiation. There is no accepted animal model for UVR-induced BCC and melanoma. 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-radiation (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 broadband UVA exposure but with low potency compared to broadband UVB (Robinson *et al.*, 2000). The observation that the relative latitude gradient of melanoma is smaller than for SCC and BCC supports the view that UVA is also involved in the induction of melanoma since the relative latitude gradient for UVA is much smaller than that for UVB (Moan *et al.,* 1999).

Melanomas have proved extremely difficult to be induced by UVR alone in mice. 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). The incidence of melanoma, as well as BCC and SCC, is very high in xeroderma pigmentosum (XP) patients with defective excision repair of UVB-type DNA damage, e.g CPD. Moreover, since sunburn appears to be an important risk factor for melanoma, UVB has been implicated in its pathogenesis (Wang *et al.,* 2001).

3.2. What are the specific health and safety implications (negative and positive) relating to the use of sun protection products during exposure of persons to solar radiation?

3.2.1. Types of sun protection

Public health programs aimed at preventing skin cancer focus almost totally on protection from sunlight. These programs usually incorporate a range of strategies, including dissemination of knowledge about the intensity of sunlight in the local environment, staying out of direct sunlight during times when the ambient intensity is high, wearing a hat and clothing on unprotected skin when in direct sunlight, and using broad-spectrum water-resistant sunscreens that protect uncovered skin from direct sunlight.

The first use of chemical sunscreens was reported in 1928. Sunscreens were first developed to protect against sunburn and were designed to filter out the burning rays of sunlight (UVB). More recently, because of evidence that longer wavelengths of sunlight (UVA) participate in the sunburn reaction and can cause skin cancer in animals, and concern that staying in the sun longer with protection against UVB increases exposure to UVA, UVA-absorbers have been added to most sunscreens to widen their absorption spectra (Gasparro *et al.,* 1998).

Topical chemical sunscreens applied to the skin act by absorbing and/or scattering incident UVR. The shape of the absorption curve is the fundamental attribute of a topical sunscreen. The active ingredients of sunscreens may be classified as organic or inorganic chemical absorbers. The organic chemical absorbers are generally aromatic compounds conjugated with a carbonyl group. One classification of such UVR absorbers (Shaath, 1997) is based on their chemical structure, as follows: cinnamates, p-aminobenzoate (PABA) derivates, salicylates, benzophenones, camphor derivatives, dibenzoyl methanes, anthranylates, and miscellaneous compounds. Cinnamates, PABA derivates, salicylates, and camphor derivatives are all principally UVB absorbers, while benzophenone derivatives, dibenzoyl methanes, and anthranylates are principally UVA absorbers. Inorganic chemical absorbers, such as titanium dioxide (TiO_2) and zinc oxide (ZnO), absorb and scatter UVR, unlike organic chemicals which only absorb. Recently, the TiO_2 and ZnO have been prepared as nanoparticles at a range of the order of 10-20 nanometres. These mineral UV filters consist of micron-sized aggregates, which are composed of nano-sized primary particles. The surface of these nanoparticles may be treated with an inert coating to improve their dispersion in sunscreen formulations. The advantage of mineral UV filters is that they have a broad absorbance spectrum.

At present an assessment of the photostability of suncare products is not a general requirement before marketing. In order to evaluate the photostability of suncare products the spectral absorbance of 16 sunscreens was measured before, and after exposure to increasing biologically weighted standard erythema doses (5, 12.5, 25, 50) of solar-simulated radiation. Seven of 16 suncare products showed a significant dose- and wavelength-dependent decrease of the UVA protective capacity, whereas the ability to absorb UVB was not affected. In the UVA range, the increase of transmission was 12 – 48% for an ultraviolet exposure of 25 SED. Photoinactivation started in the wavelength range between 320 and 335 nm with a maximum above 350 nm. Furthermore, the analysis showed that the behavior of suncare products was not predictable from its individual ingredients. Neither complex combinations of organic filters nor addition of inorganic filters could absolutely prevent photoinactivation. The inclusion of a single photounstable filter did not mean photoinstability of the complete suncare product. Photoinactivation of sunscreens appears to be an underestimated hazard to

the skin, first, by formation of free radicals, second, by increased UVA transmission (Maier *et al.,* 2001).

Photostability should be a requirement of sunscreen ingredients. Decay rates have been reported under conditions of exaggerated exposure and realistic use. Some ingredients have been reported to induce photoproducts that may cause adverse effects (Knowland *et al.,* 1993, Gulston and Knowland 1999, Butt and Christensen 2000). In general, marketed sunscreen formulations seem to be of acceptable stability today. UV-filters are not only part of sunscreen protection products, but are also used in many other cosmetic products such as hair spray, face creams and make-up. They are also used to protect e.g. paint from UV-degradation.

Before UV screens are put on the marked within EU, they are evaluated for safety by the Scientific Committee on Consumer Products (SCCP) in accordance with the SCCP's notes of guidance for the testing of cosmetic ingredients and their evaluation (SCCP, 2006b). A potentially estrogenic effect of some UV-filters has been claimed. The Scientific Committee on Cosmetic and Non-Food Products has concluded that organic UV filters used in cosmetic sunscreen products allowed in the EU market today, have no estrogenic effects that could potentially affect human health (SCCNFP, 2001).

3.2.2. Protection factors

3.2.2.1. UVB protection factors

The Sun Protection Factor (SPF) determined *in vivo* is now a universal indicator of the efficacy of sunscreen products against sunburn. A joint agreement of the international SPF Test Method was reached in October 2002 (Colipa, 2006).

The *in vivo* method evaluates protection against the short-term effects of UVB-radiation. It defines a sun protection factor (SPF) based on the ratio between the minimal erythema dose on skin protected by the product (MEDp) and the minimal erythema dose on unprotected skin (MEDu). The sunscreen (lotion, liquid, milk, cream, spray) is applied to a test area on the back of volunteers in amounts of 2 mg/cm^2. After a drying time of 15 to 30 minutes irradiation is performed with a Xenon lamp according to certain specifications. Erythema is recorded 20 $\pm$ 4 hours after exposure. Due to the reproducibility it is technical difficult to measure less than 2 mg/cm^2.

Attempts are made to develop an *in vitro* method to determine SPF (Diffey *et al.,* 2000).

3.2.2.2. UVA protection factors

No internationally accepted method for determination of UVA protection is available. The *in vivo* Persistent Pigment Darkening (PPD) method has been proposed to be used in EU.

As pointed out earlier UVA exposure results in a pigment darkening due to oxidation of melanin and its precursors. This is seen shortly after exposure and is called immediate pigment darkening (IPD). This skin pigment darkening is temporary. When exposure ends,

the color fades rapidly for 2 hours, and then more slowly for 24 hours. The skin pigment darkening observed after 2 hours is called persistent pigment darkening (PPD).

The minimal persistent pigment darkening dose for unprotected skin (MPDu) and that for protected skin (MPDp) were visually determined. MPDu and MPDp were defined as the quantity of radiant energy required to produce the first unambiguous pigmented reaction. The UVA dose required to induce an MPD corresponded to about 10 J/cm^2. The UVA protection factor of each product for each subject was then calculated based on the basis of ratio of the minimum threshold PPD dose (MPDp) on the protected site divided by the threshold PPD dose (MPDu) on the unprotected site.

The procedure is similar to determination of the SPF for UVB. The sunscreen (lotion, liquid, milk, cream, spray) is applied to a test area on the back of volunteers in amounts of 2 mg/cm^2. After a drying time of 15 to 30 minutes irradiation is performed with a Xenon lamp according to certain specifications using filters to remove UVB and visible light. The minimal persistent pigment darkening is recorded 2 hours after exposure (Moyal et al., 2000a, 2000b).

If the pigment darkening is assessed 15 minutes after exposure the method is called Immediate Pigment Darkening (IPD).

3.2.2.3. Critical wavelength method

The critical wavelength method evaluates the uniformity of the absorption spectrum of a sunscreen. The critical wavelength requires mathematical integration of the product absorbance spectrum from 290 to 400 nm to determine the wavelength below which 90% of the cumulative area of the absorbance curve resides. The method is intended to express the breadth of the absorption spectrum of the product throughout the UV domain, especially its extent in UVA. If this value is between 340 nm and 370 nm, the product is considered to offer a certain protection against UVB- and UVA-radiation. If the value exceeds 370 nm, the product is classed as “broad-spectrum” (Diffey, 1994).

3.2.3. Effectiveness of sun protection

Two types of sun exposure can be distinguished: intentional and unintentional sun exposure. Intentional exposure is that with the primary purpose of achieving a positive biological response from the sun, such as acquisition of a tan. During intentional exposure, significant portions of the trunk and limbs are frequently uncovered. Sunbathing is the most typical behavior. In children and in adults, most sunburns occur during intentional sun exposure. Unintentional sun exposure is that which occurs during daily life, during work as well as during leisure time, without the specific intention of acquiring a tan or staying in the sun for its own sake. During this type of behavior, the parts of the body that are uncovered are generally the face, ears, neck and hands.

Sunscreens were designed primarily to prevent sunburn. Use of sunscreens during unintentional exposure appears to reduce the occurrence of sunburn, but use of sunscreens or of higher-SPF sunscreens during intentional exposure appears to have little effect. One study of intentional exposure indicated that subjects who use high-SPF sunscreens stay in the sun longer than those who use lower-SPF products and that at least 'sun-seeking' populations use

sunscreen to avoid sunburn rather than total UVR exposure; guarding against skin cancer is at best a secondary motive.

In considering the effectiveness of sun protection, it should be noted that it was only in the 1990es that the sunscreen industry began offering products that provide protection against UVA as well as UVB-radiation. As late as in 1998, a report from the Annual Meeting of the American Association for the Advancement of Science questions the value of sunscreens and pointed out that some products promising UVA and UVB protection did not protect adequately against UVA. This implies that most studies considering long-term effects of sun protection may involve sunscreens that have not given adequate protection against UVA.

3.2.3.1. Positive effects

Erythema
Sun protection products offer real, documented effectiveness in preventing sunburn. However, in practice this protection may not be complete, owing to poor choice of protection index with respect to the solar UV-index, and insufficient amounts and repetition of sunscreen application.

Skin aging
The effectiveness of topical sun protection products in preventing skin aging has not yet been demonstrated in human subjects, although a few studies on prevention of skin elastosis in humans are in progress. Other studies, also conducted on humans, have shown the value of certain topical sun protection agents in preventing damage connected with light-induced aging of the skin (Fourtanier *et al.,* 1992; Séité *et al.,* 1998; Séité *et al.,* 2000). Research studies conducted on animals have shown that some UVA screens can counter light-induced aging of skin fibers in cases of chronic exposure (Takeuchi *et al.,* 1998).

Immunosuppression
Immunosuppression is a complex biological phenomenon, certainly not due to a one-way mechanism, in which the study protocol seems largely to determine the expected results. The current data is reassuring, however, sunscreens with high protection indices for UVB-radiation and, most important, for UVA-radiation provide effective protection against the decrease in cellular immune reactions observed *in vivo* after exposure to UV radiation.

Cancer
Squamous cell carcinoma
A single randomized trial has been conducted to evaluate use of sunscreens in preventing SCC (Green *et al.,* 1999). Fewer participants in the sunscreen group developed new SCC than those in the comparison group, and the total number of SCC among participants given sunscreen was lower than that in the comparison group. Only the latter difference was statistically significant.

The single cohort study (Grodstein *et al.,* 1995) showed no decrease in risk for SCC with use of sunscreens. Two case-control studies have been conducted of sunscreen use and SCC. The Australian study (English *et al.,* 1998) showed no consistent pattern of decreased risk among subjects of three different age groups using sunscreens. The Spanish study (Suarez-Varela *et al.,* 1996) showed a decrease in risk among sunscreen users, but data on BCC and SCC were

combined in the analysis. Controls for sun sensitivity and sun exposure were probably not complete in either the cohort or case–control studies.

Actinic keratoses are a recognized precursor lesion for SCC. Two randomized trials (Naylor *et al.,* 1995; Thompson *et al.,* 1993) showed significant protective effect of use of sunscreens against actinic keratoses. A cross-sectional study conducted in the United Kingdom (Harvey *et al.,* 1996a,b) was uninformative.

IARC (2001) concluded: There is limited evidence in humans for a cancer-preventive effect of topical use of sunscreen formulations against SCC.

Basal cell carcinoma
One randomized trial (Green *et al.,* 1999) of the effectiveness of sunscreens in reducing the risk for BCC was conducted in an appropriate population with appropriate measures. No protective effect on sun-exposed body sites was seen in the 4-5 years of follow-up. A single cohort study (Hunter et al., 1990) conducted among female nurses in the USA showed a small but non-significant increased risk for BCC. Two case-control studies gave contrasting results. An Australian study (Kricker *et al.,* 1995) showed a modest increase in risk among subjects using sunscreens in the 10 years prior to diagnosis. The other case–control study (Suarez-Varela *et al.,* 1996), conducted in a Spanish population, showed a lower risk among subjects using sunscreens, but data on BCC and SCC were combined in the analysis. These studies faced the same difficulties in control of confounding of sun-sensitivity factors and sun exposure as the case–control studies of melanoma.

IARC (2001) concluded: There is inadequate evidence in humans for a cancer-preventive effect of topical use of sunscreen formulations against BCC.

Cutaneous melanoma
The results of 15 case-control studies were available to evaluate the potential preventive effect of sunscreens against cutaneous melanoma. No results were available from randomized controlled trials or cohort studies. Four case-control studies (Elwood and Gallagher, 1999; Holman *et al.,* 1986; Osterlind *et al.,* 1988; Westerdahl *et al.,* 1995) provided little evidence of an effect of sunscreen use on the risk for melanoma among all subjects. Three case-control studies (Holly *et al.,* 1995; Rodenas *et al.,* 1996; Espinoza Arranz *et al.,* 1999) showed significantly lower risks for melanoma in users of sunscreens than in non-users. Two of these were relatively small, hospital-based studies conducted in populations in Spain (Espinoza Arranz *et al.,* 1999; Rodenas et al., 1996) with both a low prevalence of sun-sensitive subjects and a low prevalence of sunscreen use. The third (Holly *et al.,* 1995) was conducted among white women 25-59 years of age in California, USA. This study was unusual in showing the highest levels of risk for melanoma among women with the least solar exposure, but all of the relative risks were close to 1.0.

Eight case-control studies, in Australia, Europe and North America (Klepp and Magnus 1979; Graham *et al.,* 1985; Herzfeld *et al.,* 1993; Beitner *et al.,* 1990; Elwood and Gallagher, 1999; Autier *et al.,* 1995, 1997; Wolf *et al.,* 1998; Westerdahl *et al.,* 2000) showed significantly higher risks for melanoma in users of sunscreens than in non-users, with relative risks for the highest category of use ranging up to 2.6. When adjustment was made for sun exposure and sun sensitivity variables in five studies, the relative risk fell in two studies and changed little in three studies. However, none of the adjusted relative risks fell much, if at all, below 1.0.

In two of the studies that showed significantly increased risks for melanoma among sunscreen users, analysis of subgroups suggested that use of sunscreens during heavy intentional sun exposure was associated with a particularly high risk. One of these studies provided specific evidence that sunscreen use in such a group may have led them to prolong their sun exposure (Westerdahl *et al.,* 2000). In addition, one of the studies that showed little overall effect of sunscreens found a significantly increased risk for melanoma among people who used sunscreens only during the first hours of sun exposure (Elwood and Gallagher, 1999).

All the studies of sunscreen use and melanoma are difficult to interpret because of problems of positive confounding of sunscreen use with sun exposure, sun sensitivity and history of sun-related neoplasia and negative confounding with other sun-protective behaviour (e.g. use of protective clothing, wearing a hat or staying in the shade). None of the studies adjusted for measures of sun-related neoplasia or other sun-protective behaviour, nor was it known whether this confounding was important. Where measurement and control of sun exposure and sun sensitivity were included in the analysis, there is serious concern that they were insufficient to control confounding.

Acquired melanocytic naevi are considered to be precursors of some cutaneous melanomas. One randomized trial of the ability of sunscreens to inhibit the formation of melanocytic naevi has been published and suggests a protective effect (Gallagher *et al.,* 2000). Other evidence on this issue comes from four cross-sectional or cohort studies among children carried out in Australia and Europe. Two of these studies reported no reduction in naevus counts among children who used sunscreens when compared with children not using them (Harrison *et al.,* 1994; Luther *et al.,* 1996). The two other studies (Pope *et al.,* 1992; Autier *et al.,* 1998) reported higher naevus counts on children who used sunscreens, but the first presented no data to support this contention. In the other, the relationship persisted after attempts to control for sun sensitivity and sun exposure.

Two cross-sectional studies of melanocytic naevi have been conducted among adults. One report did not provide quantitative information on sunscreen use or the number of naevi (Dennis *et al.,* 1996). The other study showed a modest elevation in the prevalence of naevi among subjects who used ordinary sunscreens and a greater elevation among subjects who used psoralen-containing sunscreens (Autier *et al.,* 1995). The studies in adults are difficult to interpret as it is not clear whether the naevi appeared before or after use of sunscreens.

The studies of melanocytic naevi, like those of cutaneous melanoma, suffer from possible confounding of sunscreen use with sun exposure, sun sensitivity and use of other sun-protective measures and from problems of accuracy of measurement.

IARC (2001) concluded: There is inadequate evidence in humans for a cancer-preventive effect of topical use of sunscreen formulations against cutaneous malignant melanoma.

It should be noted that after the evaluation by IARC (2001) five studies have been published reporting a positive association between use of sunscreens and number of naevi (Azizi *et al.,* 2000; Darlington *et al.,* 2002; Dulon *et al.,* 2002; Wachsmuth *et al.,* 2005; Bauer *et al.,* 2005).

Comment
Sunscreens probably prevent squamous cell carcinoma on the skin when used mainly during unintentional sun exposure.

No conclusion can be drawn about the cancer-preventive activity of topical use of sunscreens against BCC and cutaneous melanoma.

Use of sunscreen can extend the duration of intentional sun exposure, such as sunbathing. Such extension may increase the risk of cutaneous melanoma.

It should be noted that the majority of the studies may have been carried out on populations that have used sunscreens providing inadequate protection against UVA.

Effects on free radical formation

Haywood and coworkers (2003) studied the efficacy of sunscreens by measuring UVA-induced free radical production. Electron spin resonance was used to detect free radicals directly in human skin during irradiation with levels of UVR comparable to solar intensities. The protection afforded by three high factor sunscreens (SPF 20+) that claimed UVA protection was examined. At application levels of $\geq$ 2 mg/cm^2 the UV-induced free radicals were reduced by only about 55% and by about 45% at 0.5 – 1.5 mg/cm^2. Thus, the "free radical protection factor" calculated on the basis of these results was only 2, which contrast strongly to the erythema-based sun protection factor. The disparity between these protection factors suggest that prolonged sunbathing would disproportionately increase exposure to UVA.

3.2.3.2. Negative effects

Vitamin D

The impact of each sun exposure on vitamin D production will depend on the area exposed, the exposure time, and the UVB intensity, which varies with latitude, season of the year, and time of day, among other factors. It has been estimated that exposure of the body in a bathing suit to 1 MED of sunlight is equivalent to ingesting about 250 μg vitamin D. As an example unintentional exposure of hands, arms, and face two to three times a week for about 5 minutes for a skin type II adult in Boston, Massachusetts in July is more than sufficient to give an adequate vitamin D level (Holick, 2001).

After applying a sunscreen with SPF 15 in an amount of 2 mg/cm^2 the time needed to produce an adequate level of vitamin D will be about 15 times longer than that without sunscreen. However, as people normally use less sunscreen, the time needed may only be 4 – 5 times longer. As discussed earlier, the action spectra for erythema and production of vitamin D are similar. However, since the main purpose of intentional sunbathing is to obtain a tan, and much higher sun exposure is needed to obtain a tan than to obtain an adequate vitamin D level, it follows that even the use of sunscreens with SFP higher than 15 during intentional sun exposure will give an adequate vitamin D level.

3.3. When and where are sun protection products used? How much and what type of sunscreen products are used?

3.3.1. Use of sunscreens

The use of sunscreens has been found to vary considerably in different studies. In a study of 360 beachgoers in Belgium, sunscreen cream was the most popular preventive behavior (use of sunscreen with SPF 15 or higher reported by 42.2%), followed by timed sun exposure (33.9%), clothing and hats (28.9%) and shade (22.2%). Forty-six percent used a sunscreen on a regular basis (every 1½ to 2 hours or after swimming or sweating), but not necessarily a SPF 15+ cream. Sunscreen use was more popular in the female population: 43.3 vs. 40.7% for sunscreen SPF 15+, and 50.7 vs. 39.3% for regular sunscreen use. The mean duration of sun exposure was 3.8 hours, with a minimum in the age group 0–3 years of 2.5 hours and a maximum in the age group 13–19 years of 4.6 hours. Twenty-three percent did not use any protective measure (Devos *et al.,* 2003).

In another study conducted among 602 Belgian adolescents, 70% reported that they did not use sunscreen regularly. Almost two-thirds of the respondents (59.3%) reported at least one sunburn in the past year and 26.5% got sunburned at least twice. Most respondents (49%) exposed themselves between 12.00 and 15.00 hours and 70% exposed themselves for at least 3 hours to the sun on sunny days (De Vries *et al.,* 2006).

In a study from England, it was found that females were more frequent users of sunscreens than males. However, only 35% females and 8% males reported regular use of sunscreens. Twenty-two per cent of the study population did not use sunscreens at all, whereas 66% of subjects bought a sunscreen product once a year or less. Thirty-four percent of the subjects reported experiencing sunburn in the last 2 years. Interestingly, more (60%) sunburns were found to occur at home in the UK than on holidays abroad, and these frequently occurred during outdoor activities other than deliberate sunbathing (Ling *et al.,* 2003).

An extensive study of sunscreen use in Denmark involved 340 volunteers, children, adolescents, indoor workers, sun worshippers, golfers, and gardeners (age range, 4-68 years). All participants carried personal, electronic UV dosimeters, measuring time-stamped UV-doses continuously, during a median of 119 days covering 346 sun-years (1 sun-year equals 1 subject participating during 1 summer season). Sunscreens were used on a median of 5 days per sun-year (range, 1 day for gardeners to 16 days for sun worshippers). Nine percent of children (4 – 15 years), 18% of adolescents (16 – 19 year), 10% of females and 41% of males never used sunscreens. Sunscreen use was not correlated with age, and children had as much unprotected risk behavior as adults. Sunscreens were used on 86% of the days with risk behavior in southern Europe vs 20% in northern Europe. A typical sunburn day in the Danish study was a day off work (91%) with risk behavior (sunbathing/exposing shoulders) (79%) in May, June, or July (90%) for 6.4 exposure hours (interquartile range, 5-7.7 hours), of which 2.8 hours fell between 12.00 and 15.00hours. Subjects had a median of 1 sunburn per sun-year; adolescents, sun worshippers, and indoor workers had more than children, golfers, and gardeners. Sunburn peaked at age 20 years, and female subjects had more sunburns than male subjects. Forty-one percent of the sunburns were characterized by redness of the skin over a small area, 39% over a moderate area, and 6% over an extensive area. Nine percent of the sunburns were reported as red and sore, and 2% were red, sore, and blistered. There was a significant association between severity and area affected. There was no significant difference in the severity of sunburn in northern vs southern Europe. No significant differences were

found between males and females in the cumulative UV-dose measured in the study period or UV-dose per day with risk behavior. The UV-doses were significantly higher on days with sunscreen and on sunburn days. The median sun protection factor was 10.5. Subject with skin types I and II applied sunscreen with higher sun protection factor (SPF 14) than those with skin types III and IV (SPF 9) (Thieden *et al.,* 2005a,b).

In a study of Danish adolescents, 48% reported having received at least one severe blistering sunburn. More Danish males than females reported sunburn (52% versus 44%). When asked how many hours were spent in the sun each day during warm weather, 72% responded 2 hours or longer. In fact, 9% reported they would spend 6 hours or more in the sun if weather permitted. Ninety percent reported use of protective sunscreen and 49% used sun protective factor (SPF) ≥ 15. (Savona *et al.,* 2005).

The number of sunscreen packages sold in Norway are approximately the same for sunscreens with SPF ≤ 8, 8 < SPF ≤ 30, and SPF > 30. However, the fact that the sale of sunscreens in the low range only increased by 2% from 2005 to 2006 while the sunscreens in the high SPF range increased by 34%, demonstrate that there are a tendency to use higher protection (personal communication from The Norwegian Association of Cosmetics, Toiletries and Fragrance Suppliers).

3.3.2. Sun protection factor and time in the sun

The question is often raised if people using high SPF stay longer in the sun than those using a low SPF sunscreen. In a double-blind randomized trial with European participants aged 18 to 24 years old, it was demonstrated that use of high SPF sunscreen could lead to longer stays in the sun (Autier *et al.,* 1999). The SPF 10 (n = 44) and SPF 30 (n = 42) groups had equivalent mean holiday durations (19.4 days versus 20.2 days) and mean quantities of sunscreen used (72.3 g versus 71.6 g). It was found that the mean daily durations of sunbathing were 2.6 and 3.1 hours, respectively, and, for outdoor activities, they were 3.6 and 3.8 hours, in the two groups respectively. There was no difference in sunburn experience between the two groups. The participants used, on average, 0.5 mg/cm^2 of the broad-spectrum sunscreens.

The study by Dupuy and coworkers (2005) examined the effect of sunscreen labeling in the real-world setting of French vacation sites in a study population consisting of 80% of middle-aged women. These investigators studied vacationers who volunteered to be randomly assigned to 3 different sunscreen groups for a week during their holiday. Participants were given SPF 40 sunscreens labeled either "*basic protection"* or "*high protection",* but were blinded as to the actual SPF. A third group got SPF 12 labeled *"basic protection"*. The end result of this study was that there was no difference in sunscreen use in the SPF 40 groups, suggesting that the "*high protection"* label did not lead to more intentional UV exposure or less sunscreen use than the same SPF 40 sunscreen labeled "*basic protection"*. These authors concluded that the policy of recommending a high SPF sunscreen is a sound one. It should be noted that these results are in contrast to the study of Autier and coworkers (1999) consisting of young students (18 to 24 years old).

3.3.3. Amount of sunscreens used

It has been asked why people who use high factor sunscreens still get sunburned? If sunscreens of sun protection factor 15 are sufficient to protect against sunburn even for all day exposure in tropical sunshine, why are people who usually or always use high factor (>15) sunscreen more likely to report sunburn than those who rarely or never use sunscreen? This question was studied by Azurdia and coworkers (1999). Ten women with long-standing photosensitivity conditions were asked to apply an intrinsically fluorescent sunscreen with SPF 15 in the manner they would normally do on a bright sunny day. Fluorescence measurements were taken from all unclothed body areas, comprising 17 sites of the head, neck, upper and lower limbs. The overall median sunscreen thickness was 0.5 mg/cm^2, with median thicknesses of individual sites ranging from 0 to 1.2 mg/cm^2. The most frequently missed sites were the posterior neck, lateral neck, and ears, all of which had median thicknesses of 0 mg/cm^2.

The protection offered by a sunscreen – defined by its sun protection factor – is assessed after it is tested *in vivo* at an application thickness of 2 mg/cm^2. In real life the amount of sunscreen applied is on average 0.5 mg/cm^2 (range: 0.25 – 1.0 mg/cm^2), independent of skin type (Wulf *et al.,* 1997; Bech-Thomsen and Wulf, 1992/1993; Neale *et al.,* 2002; Autier *et al.,* 2001; Azurdia *et al.*, 1999; Thieden *et al.,* 2005a). The formulation of the sunscreen may exhibit great variation of the spread of the active ingredients, as a more fluid formulation are not spread as evenly as a more greasy formulation, and are thus more prone not to exhibit its function (Ivens *et al.,* 2001). Autier *et al.* (2001) found no variation in sunscreen thickness according to sex, skin phototype, study place or SPF. Application thickness has a significant effect on protection. Moreover, the thickness of sunscreen on different sites may vary as indicated above.

3.3.4. Effect of amount of sunscreen used on the sun protection factor (SPF)

Recently, Faurschou and Wulf (2007) studied the relation between SPF and sunscreen thickness *in vivo*. On the backs of 20 healthy volunteers, five areas of 34 cm^2 each were marked. One area was phototested to determine the ultraviolet (UV) sensitivity. Four areas were treated with a sunscreen SPF 4 in different amounts: 0.5, 1, 2 and 4 mg/cm^2. Thirty minutes after sunscreen application, a phototest was conducted on each area. The effective SPF was calculated 22–26 hours after irradiation using the UV-dose needed to produce just perceptible erythema (minimal erythema dose) on protected and unprotected skin. The authors concluded that the relation between SPF and sunscreen quantity follows an exponential function. Application of 0.5 mg/cm^2 makes the SPF fall to the fourth root compared to 2.0 mg/cm^2 (and 1 mg/cm^2 to the square root). However, on the basis of the data presented it is not possible to assess if SPF fall as fourth root or linearly although the former relationship fits better with theoretical models of radiation penetration through absorbing and scattering material.

In Fig. 10 the apparent protection using 0.5 mg/cm^2 sunscreen compared with the SPF label is shown both assuming fourth root relationship and linear relationship. The formula $SPF_{0.5} = 1+(SPF_{2.0} -1)/4$ is used in the case of linear relationship. It is apparent that if the relationship between thickness and protection is linear, the protection obtained by using a thickness of sunscreen of 0.5 mg/cm^2 will be about 1/3 of the SPF given on the label. On the other hand, if the relationship between thickness and protection depend on the fourth root, the protection

obtained by using a thickness of sunscreen of 0.5 mg/cm^2 will only be 2.0 using a sunscreen with SPF of 15 given on the label. With a sun protection labeled SPF 30, the protection will be 2.3. Fig. 11 shows the apparent protection with a sunscreen of SPF 15 using different thickness of the sunscreen assuming a linear and an exponential relationship. It is apparent that with 1 mg/cm^2 the protection is about 50%, while with only 0.25 mg/cm^2 it is less than 20% assuming a linear relationship. With an exponential relationship the apparent protection will be even less. Thus, it will only be about 25% or SPF 4 with 1 mg/cm^2 and a little more than 10% or SPF 1.8 with 0.25 mg/cm^2. More data is, however, necessary for resolving the relationship between thickness of sunscreen applied and sun protection.

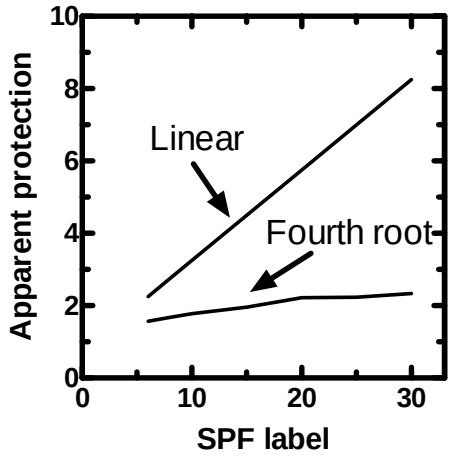


Fig. 10. *The apparent protection using 0.5 mg/cm^2 sunscreen compared with the SPF label assuming fourth root relationship and linear relationship.*

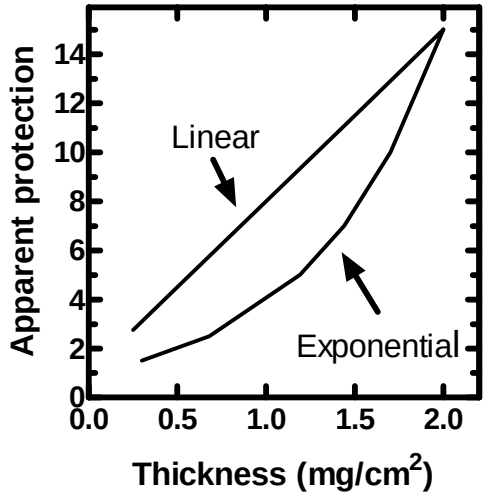


Fig. 11. *The apparent protection of different thickness of sunscreen with the SPF label of 15 assuming linear and exponential relationships.*

3.4. Are specific limit values of sunscreen protection factors to solar radiation necessary? Is it necessary to give different values for the protection factors of UVB and UVA? Give the rational for the proposed values.

3.4.1. Need for a minimum sun protection factor for UVB in sunscreens

Diffey (2002) has estimated that during adult life (18–70 years), indoor workers in the UK might typically receive 30% of their lifetime UVR exposure from sun-seeking holidays, 40% from summer weekends, 20% from casual weekday exposure between April and September, and just 10% from sun exposure during the 6-month period October to March. This indicate that year-round daily use of sunscreen products offers only a small additional benefit in reducing the annual solar UVR burden of people living in middle or north Europe compared with limiting their use to the six summer months.

People are unlikely to receive the maximum ambient exposures simply because it would be unrealistic to lie in the unshaded sun all day without moving. An extreme sunbather might spend half the time supine and half the time prone, resulting in a maximum exposure on much of the body surface of 50% of ambient. For upright people engaging in various outdoor

pursuits, such as gardening, walking, or tennis, the exposure relative to ambient on commonly exposed sites - for example, chest, shoulder, face, forearms, and lower legs, ranges from about 20% to 60%. So someone who is on vacation in southern Europe would receive a daily exposure of no more than 20 SED over much of the body surface (Diffey 2000). An exposure of 2-3 SED is necessary for a minimal erythema in the most North and Middle European skin types (II/III) (Diffey 2000).

If we consider a sunshine day in July in Oslo, the theoretical integrated dose from 09.00 to 17.00 hours is of the order 25 SED with an UV-index of 5.1 during the time period 11.00 to 14.00 hours (Fig. 3). From Table 2 it follows that an UV-index of 5 gives 4.2 SED per hour and exposure for 30 – 45 minutes may result in slight erythema. The use of a sunscreen (0.5 mg/cm^2) with SPF 6 will theoretically increase this time to about 1 – 1½ hours, while a sunscreen with SPF 15 will increase the time to 2¼ - 3 ½ hours. On the other hand an UV-index of 3 gives 2.5 SED per hour and exposure for 45 minutes – 1 hour 8minutes may result in slight erythema. The use of a sunscreen (0.5 mg/cm2) with SPF 6 will theoretically increase this time to about 1¾ – 2½ hours assuming a linear relationship between protection and thickness of sunscreen. It should be noted that if the protection decreases exponentially with the thickness of sunscreen the protection will be less. Thus, SPF 6 may be considered a minimum for a sun protection product.

Another way of argumentation may be that the lowest SPF factor on the marked should give the same protection as a tan, i.e. 2 – 3. Accordingly, as the amount of sunscreen applied corresponds to about 0.5 mg/cm^2, the protection will only be about 1/3 of the stated SPF. Thus, the lowest sun protection products available on the European marked should have a SPF ≥ 6.

Table 2. *UV-Index and standard erythema dose* (SED) (AFSSE, 2005).*

Strength of sun	**UV-Index**	**Number of standard erythema dose (SED) per hour**	**Duration of exposure corresponding to the standard erythema dose (SED)**	
			MED = 2SED	**MED = 3SED**
Weak	1	1	2h20	3h30
Weak	2	2	1h10	1h45
Average	3	2.5	45 min	1h8
Strong	4	3.5	35 min	53 min
Strong	5	4.2	30 min	45 min
Very strong	6	5	25 min	38 min
Very strong	7	6	20 min	30 min
Extreme	8	7	18 min	27 min
Extreme	9	8.5	16 min	24 min
Extreme	10	9.5	14 min	21 min

*Exposure to 2 SED – 3 SED triggers slight visible erythema in a sensitive (phototype I/II) non-acclimatized person.

3.4.2. Need for a different labeling according to sun protection factor for UVB

The question may be raised why don't manufacturers test or label sunscreens in relation to an application thickness that reflects more closely consumer usage, for example, at about 0.5 mg/cm^2? Any manufacturer would be reluctant to change without international agreement, as products currently labeled factor 20, say, would reappear with a factor of about 7, putting the manufacturer at a commercial disadvantage. Currently, consumers may be misled about sunscreen protection in a way that may impact adversely on behavior. Consequently, numerical labeling should be discontinued as it has led to more confusion than clarity. Instead sunscreen products should have qualitative measures which focus more on protection than on encouraging prolonged exposure to sunlight as indicated in Table 3. Manufacturers would continue testing products using an application thickness of 2 mg/cm^2 to determine the sun protection factor, but products would be labeled as providing low, medium, high, or very high protection. Products with protection factors of less than 6 should not be classified as sun protection products. Adults in strong sunshine (UV-index ≥ 4) should be encouraged to use high or very high protection sunscreens. Parents should be encouraged to let their children use high or very high protection sunscreens under conditions with UV-index ≥ 3.

Table 3. *Example of labeled category of sunscreen products according to measured SPF (EC, 2006)*

Labeled category	Measured SPF (according to internationally agreed methods)
Low protection	6 – 14.9
Medium protection	15 – 29.9
High protection	30 – 59.9
Very high protection	60+

3.4.3. Need for a minimum sun protection factor for UVA in sunscreens

A topical sun protection agent with a high UVB protection coefficient – an agent allowing prolonged exposure without erythema – and a "UVA protection coefficient/UVB protection coefficient" ratio less than 0.1 may offer complete protection against sunburn. However, the amount of UVA-radiation not stopped by this topical sunscreen could reach levels high enough to promote carcinogenesis. In fact, by eliminating the warning signal provided by sunburn, the highly effective erythemal protection offered by topical sunscreens with very high UVB coefficients may induce people to prolong their exposure time in the sun. Such behaviour can increase the risk of skin cancer and other adverse health effects where UVA may play a role (see section 3.3). Consequently, in order to enhance public health, it is important to ensure that the sunscreen products give sufficient protection also for UVA.

From the discussion above, it follows that some sunscreen products may actually cause damage to human health when applied under normal or reasonably foreseen conditions of use. In order to raise the level of health protection of consumers, specific limit values of sunscreen protection factors to solar radiation are necessary both for UVB and UVA, as well as for the ratio between UVA and UVB protection. Moreover, in order to ensure sufficient breadth of the absorption spectrum of the product throughout the UV domain, a critical wavelength

should be specified. The critical wavelength method evaluates the uniformity of the absorption spectrum of a sunscreen.

SPF is accepted as an indicator of UVB protection. No internationally accepted method for determination of UVA protection is available. The *in vivo* Persistent Pigment Darkening (PPD) method has been proposed to be used in EU. The critical wavelength requires mathematical integration of the product absorbance spectrum from 290 to 400 nm to determine the wavelength below which 90% of the cumulative area of the absorbance curve resides. If this value is between 340 nm and 370 nm, the product is considered to offer a certain protection against UVB- and UVA-radiation.

Limit values for SPF, PPD, and critical wavelength cannot be defined from a scientific point of use. However, specific values may be given based on different assumptions. Thus, according to the argumentation above and expressed in relation to a sunshine day in Oslo in July, it follows that a SPF of less than 6 will not give sufficient protection in the middle of the day, but may provide sufficient protection in the morning and afternoon.

The Council of Europe and the European Commission recommendation recommend that the PPD/SPF $\geq$ 1/3. It is pointed out by the Council of Europe that this ratio is based on a compromise between the precautionary principle based on clinical considerations, the recommendations of the American Academy of Dermatology (AAD), the technological capacities of the filters, and quantification methods. The value of the critical wavelength should exceed 370 nm in order to be accepted as a "broad-spectrum" sunscreen.

The sunscreen industry began offering products protecting against UVA as well as UVB in the 1990es. However, even today a number of products promising UVA and UVB protection does not protect adequately against UVA. Ten years ago, most commercially available sunscreen products had sun protection factors of less than 10, but today there is a trend for higher factors. Most manufacturers make products with SPF of 15 to 20, and it is not uncommon to find products claiming a factor of 50 or higher.

As late as in 2006, a Norwegian study of 15 different sunscreen preparations revealed that 3 of the products (20%) did only give little or no UVA protection. Six of the products tested (40%) did not satisfy the Commission recommendation of 22 September 2006 on the efficacy of sunscreen products (National Veterinary Institute, 2006). These results clearly demonstrate the need for regulation of the sunscreen marked.

4. CONCLUSIONS

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

The purpose of sunbathing is to achieve a tan. Many people claim that sunbathing makes them feel good. Clinically relevant UVR from exposure to solar radiation is UVB (280 – 320 nm) and UVA (320 – 400 nm). The internationally agreed UV-index (UVI) scale is defined in terms of the erythemally weighted irradiance (i.e. the intensity contributing to skin reddening). It is intended for use for information purposes towards the general public to indicate the level of photo protection needed for a given location and time. UVB penetrates only a few micrometers (μm) in the skin and is primarily responsible

for inducing erythema (sunburn) and tanning while UVA can go through the epidermis and irradiate underlying tissues. It is assumed that UVA contributes in a typical mid-day solar spectrum to about 15 – 20% of sunburn. 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, phototype I being the most sensitive, and phototype VI being the most resistant. Moles and freckles are good indicators of susceptibility to malignant melanoma and are independent risk factors for skin cancer. Exposure of the skin to UVR results in skin ageing known as photoageing. UVR is immunosuppressive in humans, the consequences of which are unknown but may be important in skin cancer and infectious diseases. Solar UVR, especially UVB, causes photokeratitis (snow blindness) of the eye and contributes to cataract formation. There is evidence that solar UVR exposure is associated with ocular melanoma. Sun exposure is the most important source of vitamin D formation. The production of vitamin D in the skin is dependent on many factors, such as pigmentation, age, use of sunscreen, season of the year, latitude, surface reflection, thickness of the ozone layer and weather. The ability of the skin to produce vitamin D is reduced at increasing age.

2. What are the specific health and safety implications (negative and positive) relating to the use of sun protection products during exposure of persons to solar radiation?

Public health programs aimed at preventing skin cancer focus on protection from sunlight. They incorporate a range of strategies, including using broad-spectrum sunscreens that protect uncovered skin from direct sunlight. Sunscreens were first developed to protect against sunburn and were designed to filter out UVB. More recently, substances that filter out UVA have been added to sunscreens. The sun protection factor (SPF) against UVB determined *in vivo* is now a universal indicator of the efficacy of sunscreen products. No internationally harmonised method for determination of UVA protection is available. The *in vivo* Persistent Pigment Darkening (PPD) method has been proposed to be used in EU. The critical wavelength method evaluates the uniformity of the absorption spectrum of a sunscreen. It requires mathematical integration of the products absorbance spectrum from 290 to 400 nm to determine the wavelength below which 90% of the cumulative area of the absorbance curve resides. Before UV screens are put on the marked within EU, they are evaluated for safety by the Scientific Committee on Consumer Products (SCCP) in accordance with the SCCP's notes of guidance for the testing of cosmetic ingredients and their evaluation. A potentially estrogenic effect of some UV-filters has been claimed. The Scientific Committee on Cosmetic and Non-Food Products (SCCNFP) has concluded that organic UV filters used in cosmetic sunscreen products allowed in the EU market today, have no estrogenic effects that could potentially affect human health. Sun protection products offer real, documented effectiveness in preventing sunburn. The effectiveness of topical sun protection products in preventing skin aging has not yet been demonstrated in human subjects. Sunscreens with high protection indices for UVB-radiation and, most important, for UVA-radiation provide effective protection against the decrease in cellular immune reactions. Sunscreens probably prevent squamous cell carcinoma in the skin. No conclusion can be drawn about the cancer preventive activity of topical use of sunscreens against basal cell carcinoma and cutaneous melanoma. It

should be noted that the majority of the studies may have been carried out on populations that may have used sunscreens providing inadequate protection against UVA. Since the main purpose of sunbathing is to obtain a tan, and much higher sun exposure is needed to obtain a tan than to obtain an adequate vitamin D level, it follows that even the use of sunscreens with high SPF will give an adequate vitamin D level.

3. When and where are sun protection products used? How much and what type of sunscreen products are used?

More females than males use sunscreens. Unprotected risk behaviors (e.g. sunbathing or exposing shoulders without sun protection) occur both among children and adults. One study showed that females had more unprotected risk behavior than males. Fortunately, risk behavior seemed to be less on vacations to South Europe than in the home country. The use of sunscreens appeared to be higher on vacation to the south Europe than at home. Sales numbers from Norway indicates that the sale of sunscreens with high SPF increases most. Sunscreens with SFP 15+ seem to be most popular. The average amount of topical sunscreen actually applied by users (0.5 or even 0.25 mg/cm^2) is far below the amount recommended for the technical evaluation of protection coefficients (2 mg/cm^2), thus the average protection is probably only 1/3 of the SPF given for the sunscreen used if it is assumed that there is a linear relationship between thickness of sunscreen and protection. If there is an exponential relationship, which has also been suggested, the protection will only be about 13% of the SPF given. Thus, studies are needed to establish the relationship between thickness of sunscreen applied and sun protection. Moreover the amounts used at different sites of the body may vary between 0 and 1.2 mg/cm^2. A large number of sunbathers experience sunburn. This may in part be due to unprotected risk behavior and in part to differences in the thickness of the sunscreen applied at different sites of the body. Sunburns appear to occur more often on days off work in the home country than on vacation to the south.

4. Are specific limit values of sunscreen protection factors to solar radiation necessary? Is it necessary to give different values for the protection factors of UVB and UVA? Give the rational for the proposed values.

As late as in 2006, a Norwegian study of 15 different sunscreen preparations revealed that 3 of the products (20%) did only give little or no UVA protection. Six of the products tested (40%) did not satisfy the EU Commission recommendation on the efficacy of sunscreen products. These results clearly demonstrate the need for a stronger regulation of the sunscreen market. Numerical labeling with SPF of sun protection products should be discontinued as it has led to more confusion than clarity. Instead the products should have qualitative messages with focus on protection. The use of SPF may have encouraged some individuals to prolong their exposure to sunlight. Manufacturers would continue testing products using an application thickness of 2 mg/cm^2 to determine the sun protection factor, but products could be labeled as providing low, medium, high, or very high protection. In terms of public health, it is important to raise public awareness of potential adverse health effects from sunbathing. Adults in strong sunshine (UV-index $\geq$ 4) would be encouraged to use high or very high protection sunscreens. Parents should be encouraged to let their children use high or very high protection sunscreens under conditions with UV-index $\geq$ 3. Products with SPF for UVB protection of less than 6 should not be classified as

suns protection products as they do not provide any practical protection. With regard to UVA, the Council of Europe and the EU Commission recommend that the PPD/SPF ≥ 1/3. It is pointed out by the Council of Europe that this ratio is based on a compromise between the precautionary principle based on clinical considerations, the recommendations of the American Academy of Dermatology (AAD), the technological capacities of the filters, and quantification methods. The value of the critical wavelength should exceed 370 nm in order to be accepted as a "broad-spectrum" sunscreen giving sufficient UVA protection.

5. RECOMMENDATIONS

1. *The Sun Protection Factor (SPF) determined in vivo (Colipa 2006) should be used as indicator for UVB protection.*

2. *The persistent pigment darkening (PPD) determined in vivo should be used as indicator for UVA protection.*

3. *The persistent pigment darkening (PPD) determined in vivo should be further developed with the aim of obtaining an international agreement for the method and the analytical procedure.*

4. *The term "sun protection products" and similar terms indicate that the product protects both against UVB and UVA. The protection against UVB should correspond to SPF ≥ 6. The protection against UVA should correspond to the ratio PPD/SPF ≥ 1/3, and the value of the critical wavelength exceeding 370 nm.*

5. *The following terms should be used to indicate the protection against erythema: Low protection (6.0 ≤ SPF ≤ 14.9); Medium protection (15.0 ≤ SPF ≤ 29.9); High protection (30.0 ≤ SPF ≤ 59.9); Very high protection (60.0 ≤ SPF).*

6. *Studies are needed to establish the relationship between thicknesses of sunscreen applied and sun protection.*

7. *It is desirable to develop internationally harmonised in vitro methods for determination of sun protection.*

6. MINORITY OPINION

Not applicable.

7. GLOSSARY

BCC - basal cell carcinoma
IARC - International Agency for Research on Cancer
IPD - minimal immediate pigment darkening
MED - minimal erythema dose
MEDp - minimal erythema dose measured in the presence of 2 mg/cm^2 sunscreen preparation

MEDu - minimal erythema dose measured in the absence of sunscreen preparation
MPD - minimal persistent pigment darkening
MPDp - minimal persistent pigment darkening measured in the presence of 2 mg/cm^2 sunscreen preparation
MPDu - minimal persistent pigment darkening measured in the absence of sunscreen preparation
OR - odds ratio
PPD - persistent pigment darkening (MPDp/MPDu)
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 (MEDp/MEDu)
UVA - ultraviolet radiation with wavelengths 320–400 nm
UVB - ultraviolet radiation with wavelengths 280–320 nm
UVC - ultraviolet radiation with wavelengths < 280 nm
UVI - ultraviolet index, (UV-index)
UVR - ultraviolet radiation

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