

I very much appreciated the opportunity to give my perspective on the potential health benefits from exposure to ultraviolet B, ultraviolet A, and visible radiation. I have been conducting research in the field of the photobiology of vitamin D for more than 40 years. My laboratory established how vitamin D is produced in the skin during sun exposure and investigated various factors including aging, latitude, skin pigmentation, sunscreen use, altitude, time of day and season of the year on the cutaneous production of previtamin D3.

Please find below my comments regarding the SCENIHR preliminary opinion on sunbeds.

Page 10, lines 23-24 and Page 32, lines 11-12

It's been suggested that exposure to a sunbed results in a decrease in vitamin D3 in the skin because of photo-destruction. What we had previously demonstrated was during exposure to natural sunlight and artificial UVB radiation, 7-dehydrocholesterol absorbs the energy and is converted to previtamin D3. We have found that when human skin is exposed to sunlight this process is immediately initiated. The 7-dehydrocholesterol is efficiently converted to previtamin D3. Once formed previtamin D3 can absorb UVB radiation and is converted into 2 major photoisomers: lumisterol and tachysterol. These photoisomers absorb UVB radiation and are converted into previtamin D3. As a result, a photoequilibrium is established. Thus during exposure to UVB radiation there continues to be an increase in previtamin D3 levels in the skin that reaches a photoequilibrium plateau when about 10-15% of 7-dehydrocholesterol is converted to previtamin D3. (Holick MF, MacLaughlin JA, and Doppelt SH. Regulation of cutaneous previtamin D3 photosynthesis in man: Skin pigment is not an essential regulator. Science. 1981. 211:590-593; MacLaughlin JA, Anderson RR, Holick MF. Spectral character of sunlight modulates the photosynthesis of previtamin D3 and its photoisomers in human skin (Science. 1982. 1001-1003). The amount of sunlight required to accomplish this is equivalent to more than 4 MEDs of UVB exposure. We also demonstrated that healthy adults exposed to 1-4 MEDs of UVB exposure in a sunbed demonstrated a continued dose dependent increase in circulating blood levels of vitamin D3 (Adams JA, Clemens TL, Parrish JA, and Holick MF. Vitamin-D synthesis and metabolism after ultraviolet irradiation of normal and vitamin-D-deficient subjects. N Engl J Med. 1982. 306(12):722-725.).

Therefore it is with a high degree of scientific certainty that the concept that vitamin D is destroyed when being exposed to a sunbed is completely inaccurate.

The SCHEER acknowledges the constructive comments. The text on vitamin D has been amended.

Page 6, lines 32-34 and Page 10, lines 22-37,

We also reported in the same study that patients with severe fat malabsorption benefited from exposure to ultraviolet B radiation by improvement in their blood levels of vitamin D and 25-hydroxyvitamin D (a measure of vitamin D status). We separately published an additional study demonstrating the effectiveness of a sunbed in correcting the calcium metabolism disorder in a patient with severe Crohn's disease who had uncompromising aches and pains in her bones and muscles due to the vitamin D deficiency. Exposure to a sunbed UVB radiation markedly increased her blood level of 25-hydroxyvitamin D and she had complete resolution in the excruciating pain that was associated with vitamin D deficiency and associated osteomalacia.

(Koutkia, P., Lu Z., Chen, T.C., and Holick, M.F. Treatment of vitamin D deficiency due to Crohn's disease with tanning bed ultraviolet B radiation. Gastroenterol. 2001. 121:1485-1488.)

The treatment of medical conditions is outside the scope of the mandate. No change of the text of the Opinion needed.

Page 6, lines 33-34 and Page 10, lines 26-28 and Page 34, lines 17-18

We conducted a study in tanners in Boston comparing not only their blood levels of 25-hydroxyvitamin D but also their bone mineral density in their hip and spine compared to sex and age matched healthy adults who have never been exposed to a sunbed. The study was conducted in the winter. We reported that all of the healthy adults controls were vitamin D deficient or insufficient with an average blood level of 25-hydroxyvitamin D of 18 ng/mL whereas the tanners had on average a blood level that was considered to be robust at 48 ng/mL; a level similar to what has been reported in Maasai Warriors who live outdoors and are exposed to sunlight on a daily basis. (Tangpricha, V. Turner, A., Spina, C., Decastro, S., Chen, T., and Holick, M.F. Tanning is associated with optimal vitamin D status (serum 25-hydroxyvitamin D concentration) and higher bone mineral density. *Am J Clin Nutr.* 2004. 80:1645-1649; Luxwolda MF, Kuipers RS, Kema IP, Dijck-Brouwer DA and Muskiet FAJ: Traditionally living populations in East Africa have a mean serum 25-hydroxyvitamin D concentration of 115 nmol/l. *Br J Nutr* 108: 1557-1561, 2012.) In addition we found that the bone density in the hip of tanners was statistically significantly higher compared to the control adults.

There has been a lot of discussion about the role of sunlight and maintenance of your vitamin D status. We reported on 3.8 million samples throughout the United States on circulating blood levels of 25-hydroxyvitamin D throughout the year. The data clearly demonstrate that the lowest blood levels of 25-hydroxyvitamin D occur at the end of the winter whether you live in the southern, middle or northern United States and that these levels are considered to be vitamin D deficient or insufficient. The peak blood levels occur the end of the summer and these peak levels are the same from the samples obtained in the southern, middle and northern United States and on average were considered to be vitamin D insufficient with the 25-hydroxyvitamin D of 29 ng/mL. (Kroll, M. Bi, C, Garner, C, Kaufman, H, Liu, D, Holick, MF. Temporal Relationship between Vitamin D Status and Parathyroid Hormone in the United States 2015 Mar; 10(3). *PLoS One.* pone.0118108.)

The Opinion clearly states that exposure to sunlight and exposure from sunbeds enhance vitamin D levels. A full discussion on what is an adequate serum level is outside the scope of the mandate. No change of the text of the Opinion needed.

Page 10, lines 32-35 and Page 32, lines 27-46 and Page 33, lines 1-21

There is an extensive literature on other biologic effects of UVB, UVA and visible radiation that occurs in the skin. I've recently reviewed many of these effects that I have provided to the committee. (Holick, MF. Biologic effects of sunlight, ultraviolet radiation, visible light, infrared radiation and vitamin D for health. *Anticancer Research* 2016. 36; 1345-1356.) It is true that UVB and UVA radiation causes immunosuppression and immunotolerance. This well documented effect on the immune system likely is important and helps explain the many observations demonstrating that living at lower latitudes or having higher circulating levels of 25-hydroxyvitamin D is associated with reduced risk of many autoimmune diseases including type 1 diabetes, multiple sclerosis, rheumatoid arthritis and Crohn's disease. A recent study demonstrated in a mouse model that exposure to UVB radiation was more effective than the vitamin D in reducing the risk of developing an encephalitis is similar to multiple sclerosis in humans.

A full discussion on the association between outdoor sunlight exposure, latitude and various health parameters is complex and outside the scope of the mandate, which is on exposure to sunbeds per se. No change of the text of the Opinion needed.

Page 33, lines 42-46 and Page 34, lines 1-13

People feel better when they are exposed to sunlight and feel more relaxed. It is reported in the literature that exposure to UVB and UVA radiation increases the production of beta endorphin in keratinocytes in the skin that results in an increase in beta endorphin levels in the circulation. People who live near the equator have a lower blood pressure than those living at higher latitudes. Both blood pressure and cardiac mortality are at their highest level at the end of the winter. Exposure to UVA radiation not only increases the production of nitric oxide in keratinocytes but also introduces its release from keratinocytes. Nitric oxide is a major factor for regulating blood pressure causing vasodilation of the vasculature thereby resulting in a lower blood pressure. It is also been reported that exposure of the heme molecule to ultraviolet radiation results in the release of carbon monoxide which is known to also be a vasodilator and to have a variety of other beneficial effects including acting as a neurotransmitter.

Text on blood pressure and beta endorphin has been added to the document.

Page 33, lines 11-16

Exposure of skin and skin cells to ultraviolet radiation results in an increase in the expression of the proopiomelanocortin gene. This gene is responsible for producing ACTH, which can travel to the adrenal glands increasing the production of cortisol. This may be another explanation for why being exposed to the most sunlight and living at lower latitudes reduces risk for autoimmune diseases including rheumatoid arthritis. It may also help in reducing some of the symptoms associated with rheumatoid arthritis.

As mentioned above, a full discussion on the association between outdoor sunlight exposure, latitude and various health parameters is complex and outside the scope of the mandate, which is on exposure to sunbeds per se. No change of the text of the Opinion needed.

Page 32, lines 28-30

Visible radiation is now being used for enhancing wound healing and improving the structural integrity of the skin.

As mentioned above, the treatment of medical conditions is outside the scope of the mandate. No change of the text of the Opinion needed.

Page 6, lines 26-28 and Page 10, lines 39-42

There is no question that excessive exposure to sunlight increases risk for nonmelanoma skin cancer. What is remarkable is that the most deadly skin cancer, melanoma, occurs on the least sun exposed areas and occupational sun exposure reduces risk for this deadly disease. (Kennedy C, Bajdik CD, Willemze R, De Gruijl FR, Bouwes and Bavinck JN: The influence of painful sunburns and lifetime sun exposure on the risk of actinic keratoses, seborrheic warts, melanocytic nevi, atypical nevi, and skin cancer. J Invest Dermatol 120: 1087-1093, 2003.) The most important factors for increasing risk for this deadly cancer include genetic susceptibility, number of sun burning experiences, especially as a child and young adult, large number of moles on the body and being red headed and therefore prone to being sunburned.

An extensive discussion on the literature about evidence of skin cancer risk attributable to exposure to sunbeds per se, which is the focus of the mandate, can be found in the Opinion.

Page 6, lines 32-34 and Page 10, lines 22-31 and Page 34, lines 15-20

Obtaining sensible sun exposure has many health benefits as I have reviewed with the committee. People who choose to tan indoors are likely receiving many of the same health benefits as being exposed to sunlight. The amount of UVB radiation being emitted by a sunbed is effective in producing vitamin D in the skin to maintain healthy levels of 25-hydroxyvitamin D. These healthy levels have been associated with a reduced risk for developing many chronic serious illnesses including autoimmune diseases, cardiovascular disease, stroke, type 2 diabetes, infectious diseases, depression and your cognitive dysfunction. (Hossein-nezhad A and Holick MF: Vitamin D for Health: A Global Perspective. Mayo Clin Proc 88(7): 720-755, 2013.) In addition exposure of the skin to UVB, UVA and visible radiation has a plethora of well documented photochemically-induced beneficial effects.

Thus the committee should give careful consideration when weighing the scientific evidence for health benefits from exposure to suberythemal doses of simulated sunlight in a tanning-sun bed to the negative health consequences that can occur from exposure to this radiation. In my opinion the verdict is still out on whether exposure to suberythemal doses of UVB radiation in a tanning bed increases risk for melanoma. From my reading of the literature, what appears to be most important in reducing risk for melanoma is to avoid sunburning especially as a child and young adult.

Furthermore since occupational sun exposure reduces risk for melanoma it would seem reasonable that a person exposed to a tanning-sun bed to an amount of UV radiation that does not cause sun burning but tanning, thereby mimicking occupational sun exposure, would either have no increased risk or possibly even a reduced risk for developing melanoma.

A full discussion on the association between sunlight exposure (which is different from exposure from sunbeds), vitamin D and health effects is outside the scope of the mandate. The opinion reviews all documented effects from exposure to sunbeds per se, including the attributable risk of melanoma. No change of the text of the Opinion needed.