Maisons-Alfort, April 20, 2016

Public consultation on the Preliminary Opinion on the Health Effects of Sunbeds

Anses comments on SCENIHR's opinion on sunbeds 3rd December 2015

Chapters/sections: /

Comment: First of all, the document is well documented and provides very strong conclusions. The overall document presents an exhaustive up-to-date evaluation of the scientific knowledge both from human and animal studies on the potential risks from sunbed use.

Chapters/sections: Abstract, p4, lines 7-9, p9, lines 10-12

Comment: It should be reminded that the full UV spectrum UVA, UVB, UVC was evaluated by IARC based on much more data stemming from human and animal studies. The level of evidence for such an association is particularly high and IARC classified the whole UV spectrum as carcinogen. Because of the specific emission of artificial tanning devices, which are emitting particularly intense UV exposure, and based on several human and animal studies which are covered by SCENIHR report, the IARC added also UV-emitting devices in the group classification.

Chapters/sections: Abstract, p5, Health effects: non-cancer health effects AND p10 Executive summary; Chapter 1.4 Health Effects: Non-cancer health effects AND p31-34 Main report; Chapter 7 Health Effect, Introduction and Summary of the chapter 7.1 Non-cancer health effects

Comment: The SCENHIR Opinion is a very substantial review on the adverse effects (vitamin D and immunosuppression). However, some of them are poorly described or not at all:

- Effects on the eyes;
- Effects on the skin;
- Metabolic effect;
- Behavior, Addiction;
- Other.

We propose some references to argue these elements, there may be others (this list is not exhaustive):

Anses. Rayonnements ultraviolets – état des connaissances sur l'exposition et les risques sanitaires [internet]. Anses. Maisons-Alfort. 2005. [cited 2016 Mar 25]. Available from:https://www.anses.fr/fr/system/files/AP2004et7183Ra.pdf

Ernst A, Grimm A, Lim HW. Tanning lamps: health effects and reclassification by the Food and Drug Administration. J Am Acad Dermatol. 2015 Jan;72(1):175-80. doi: 10.1016/j.jaad.2014.10.016.

Hickle A, Forster J, Lazovich D, et al. Sanitarians' work with indoor-tanning businesses: findings from interviews in two major metropolitan areas. J Environ Health. 2005;67(8):30-36, 54.

International Agency for Research on Cancer, World Health Organization. Exposure to Artificial UV Radiation and Skin Cancer. Lyon, France: International Agency for Research on Cancer; 2006. http://www.iarc.fr/en/publications/pdfs-online/wrk/wrk1/ArtificialUVRad&SkinCancer.pdf. Accessed July 10, 2013

Lucas RM, McMichael AJ, Armstrong BK, et al. Estimating the global disease burden due to ultraviolet radiation exposure. Int J Epidemiol. 2008;37(3):654-667.

National Electronic Injury Surveillance System, All Injury Program. National estimates for tanning bed/booth-related injuries, 2003–2012. Analyzed by National Center for Injury Prevention and Control and National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention. Unpublished data, analyzed 2014.

World Health Organization. Ultraviolet radiation and the INTERSUN programme: the known health effects of UV. World Health Organization website. http://www.who.int/uv/faq/uvhealtfac/en/index1.html . Accessed December 3, 2013.

Effects on the eyes: UV exposure can have adverse effects on the eyes, affecting surface tissues and internal structures (cornea and lens) with acute and chronic effects. Short-term eye damages including eye irritation, photokeratitis (sunburn of the eye) and conjunctivitis can occur, but also acute corneal perforation, pterygium and solar retinopathy. Long-term eye damages include the formation of cataracts, but also macular degeneration or pinguecula.

Wearing sunglasses that fit properly and have 100% UVA and UVB protection is the best way to protect eyes from UV damage. Closing the eyelids cannot replace eye protection with UV filtration.

Effects on the skin: In addition to increasing the risk of skin cancer, UV exposure can have other adverse effects on the skin. Excessive UV exposure can cause premature skin aging, including wrinkling, mottled pigmentation (freckling or lentigines), and loss of elasticity. Excessive UV exposure can increase the risk of actinic keratosis; it is also known as solar keratosis.

Quatresooz P, Henry F, Paquet P, et al. Photoaging under recreational sunbeds. Skin Res Technol. 2011;17(3):309-313.

Metabolic effect: Excessive UV exposure may reduce the effectiveness of folic acid supplements, which has potential health consequences for pregnant women and women of childbearing age.

Borradale D, Isenring E, Hacker E, et al. Exposure to solar ultraviolet radiation is associated with a decreased folate status in women of childbearing age. J Photochem Photobiol B. 2014;131(5):90-95.

Behavior, Addiction: Behavior and addictions were not included in the searches for the literature review (cf. annex 1, p 66). The authors cited Hillhouse JJ et al for the prevalence of sunbeds among teenagers in USA (cf. Annex III, page 79) but not for evaluating a measure of tanning abuse and dependence, the purpose of this study. Hillhouse JJ et al developed the Structured Interview for Tanning Abuse and Dependence (SITAD) modified items from the Structured Clinical Interview for DSM-IV Axis I Disorders that focus on opiate abuse and dependence. More recently, Heckman and colleagues (2014) have also introduced another instrument called the Tanning Pathology Scale (TAPS) to identify cases of tanning dependence. The newly developed SIDAT and TAPS criteria should also be tested. They could possibly provide researchers with more valid alternatives to the commonly used mCAGE score, often used to prove the existence of tanning dependence, which does not appear to be a valid instrument. There is enough scientific evidence that tanning can be also included in the spectrum of addictive behaviors. However, other studies are required to determine the validity of an addiction diagnosis and to explore

pharmacologic and cognitive therapeutic options for affected persons. Further controlled studies must be performed, especially in neurobiology and imaging, to improve our understanding of tanning dependence.

We propose some references to argue these elements, there may be others (this list is not exhaustive):

Ashrafioun L, Bonar EE. Tanning addiction and psychopathology: Further evaluation of anxiety disorders and substance abuse. J Am Acad Dermatol. 2014 Mar;70(3):473-80. doi: 10.1016/j.jaad.2013.10.057.

Heckman CJ[1], Darlow S, Kloss JD, Cohen-Filipic J, Manne SL, Munshi T, Yaroch AL, Perlis C. Measurement of tanning dependence. J Eur Acad Dermatol Venereol. 2014 Sep;28(9):1179-85.

Hillhouse JJ, Baker MK, Turrisi R, et al. Evaluating a 17 measure of tanning abuse and dependence. Arch Dermatol. 2012; 148:815–819

Kourosh AS, Harrington CR, Adinoff B. Tanning as a behavioral addiction. Am J Drug Alcohol Abuse. 2010 Sep;36(5):284-90. doi: 10.3109/00952990.2010.491883.

Petit A, Lejoyeux M, Reynaud M, Karila L. Excessive indoor tanning as a behavioral addiction: a literature review. Curr Pharm Des. 2014;20(25):4070-5.

Reed DD. Ultra-violet indoor tanning addiction: a reinforcer pathology interpretation. Addict Behav. 2015 Feb;41:247-51. doi: 10.1016/j.addbeh.2014.10.026.

Other: In addition, indoor tanning can cause burns to the skin and if tanning devices are not properly sanitized, skin infections.

Russak JE, Rigel DS. Tanning bed hygiene: microbes found on tanning beds present a potential health risk. J Am Acad Dermatol. 2010;62(1):155- 157.

Chapters/sections: Abstract, p6 line21, p11 line 40, p59 lines 12-14

Comment: The updated meta-analysis by Boniol *et al.* (2012), reported an increased risk of 59% of cutaneous melanoma attributable to sunbed use for first use of sunbed before the age of 35, slightly lower than the initial evaluation by IARC in 2006. Because Boniol *et al.* (2012) meta-analysis is more recent, includes more studies, and has been conducted by the same team as IARC 2006, it would be preferable to report the figure of 59% instead of 75%. Based on figures in the meta-analysis of Boniol *et al.* (2012) with a relative risk of 1.59, this fraction would be 37% of melanoma cases caused by sunbeds use among individuals who exposed themselves to sunbeds before the age of 35.

Chapters/sections: Abstract, p6, lines 25-37 - Overall conclusion

Comment: Anses agrees with the overall Scenihr conclusion. Since 2012, ANSES therefore recommends the cessation, ultimately, of all commercial use of tanning by artificial UV rays and of the sale of appliances emitting artificial UV rays for cosmetic purposes (see OPINION of the French Agency for Food, Environmental and Occupational Health & Safety relating to a draft decree concerning the sale and provision to the public of certain tanning devices that use ultraviolet radiation available online in English: https://www.anses.fr/en/system/files/AP2012sa0263EN.pdf).

Chapters/sections: Abstract, p6 lines 30-31, p11 lines 41-42, p12 lines 4-5, p59 lines 15-17, p60 lines 41-44

Comment: There is a misunderstanding of the aetiologic fraction which corresponds to the fraction of cases caused by sunbed use among exposed population. The age level of 35 corresponds to the age at exposure and not the age at diagnosis of melanoma. The

estimation of 76% in Cust *et al.* (2011) and 43% in Boniol *et al.* (2010), is therefore to be interpreted as an estimation of the proportion of melanoma cases caused by sunbeds among those individuals who exposed themselves to sunbeds for the first time before the age of 35.

Chapters/sections: Abstract, p6, lines 32-34 - Overall conclusion

Comment: You write that '*the small potentially beneficial effects of sunbed use are more than outweighed by the many severe adverse effects*' but you do not indicate the potentially beneficial effects. Which are they? We find this sentence ambiguous. Beneficial effects, if any, should be clearly stated and described.

Anses agree with this statement: '*There is no need to use sunbeds* […]'.

It has been published that the exposure of 6-10% of the body surface (hands, arms and face) to half of a MED (5 min, skin-type-2 adult) two or three times a week is more than adequate. Doses needed to synthesize vitamin D are not enough to get a tan. Moreover, external vitamin D supplements can help, lowering the need for UVR exposure.

We propose some references to support these elements, there may be others (this list is not exhaustive):

Egan KM, Sosman JA, Blot WJ. Sunlight and reduced risk of cancer: is the real story vitamin D? J Natl Cancer Inst. 2005 Feb 2;97(3):161-3.

Holick MF. Sunlight Dilemma: risk of skin cancer or bone disease and muscle weakness. Lancet. 2001 Jan 6;357(9249):4-6

Chapters/sections: § 1- Executive summary, p10, lines 9-20; p25, lines 11-45 and p26, lines 1-33

Comment: The prevalence data are limited to Western Europe. There is no mention of data from central European countries. Because of the European status of SCENIHR, it would be worth mentioning this lack of data and calling for evaluation of prevalence in central European countries, in particular because of the presence of fair skin populations with an equally high risk of death from melanoma as compared to western countries.

Chapters/sections: § 1- Executive summary, p10, lines 21-37

Comment: There is no mentioning of accidents and side-effects like severe sunburns which sometimes occur after sunbed use. Although there is no systematic study of these events, many epidemiological studies report sunburn occurring with sunbed use and could be considered as a marker of risk, even though hardly quantifiable.

Chapters/sections: § 1- Executive summary, p11, lines 5-6; p42, lines 22-31

Comment: It should be noticed that despite sunbed use were self-reported, studies could show that the increased risk were not due to a particularly old or recent generation of tanning devices. In addition, these sunbeds clearly corresponded to cosmetic use to acquire a tan as the great majority of studies excluded use of UV-emitting devices for medical reasons.

Chapters/sections: § 1- Executive summary, p11, lines 26-27

Comment: The importance of UVA is clearly identified by the authors who wrote several times "*Importantly, UVA has been shown to be at least as much involved as UVB in DNA damage and mutation induction".* This may be a bit an overstatement. For the different biological endpoints related to cancer (DNA damage, mutagenesis), UVA is 2 to 3 orders of magnitude less efficient than UVB. It can thus be estimated that the contribution of UVA to the deleterious effects of sunbeds is at the most in the range of 10 to 20%. It could be counter-productive if this kind of sentence were used against the rest of the text that is of very high quality.

Chapters/sections: § 2- Background, p14, lines 34-39

Comment: Most regulations provide a technical framework for artificial tanning equipment control, set limit values for artificial UV irradiance from equipment and prohibit its use by those less than 18 years of age. However, the high UV doses allowed, the lenient restrictions on use, especially for sensitive persons, and the lack of resources available to the units in charge of inspection, make it impossible to reduce the number of health events associated with the use of sunbeds. Moreover, the fact that it is the service personnel in tanning studios who are assigned of information and prevention measures is not efficient.

Thus, it becomes necessary to find new ways of implementing an effective public health policy.

Chapters/sections: § 5.3- Regulations and standards, Regulation of sunbed use, p22, lines 37-38

Comment: It is written "This decree was reinforced in 2013 (Decree n°38 2013-1261 of 27 December 2013)". You could complete with examples: the maximum annual dose shall not exceed 10 kJ/m² (previously 15 kJ/m²) and the initial inspection of tanning equipment must now be carried out before making it available to the public (previously there was only a technical control every 2 years).

Chapters/sections: § 5.3- Regulations and standards, Regulation of sunbed use, p22

Comment: Medical Device (MD) are defined in the Council Directive 93/42/EEC of 14 June 1993 (medical devices are used to diagnose, prevent, monitor, treat, *etc*.). Products can also be medical devices if a medical claim is being made by the manufacturer for the device, although these products are usually not. If potentially beneficial effects of sunbed use are mentioned by the industry (cf. discussion on vitamin D §7), then, such devices should be considered as medical devices (Class IIa). Therefore, they should respect the specific regulation and be submitted to authorization. Clinical trials should be done also in order to support a reasonable assurance of safety and effectiveness for the marketing application…

The Council Directive also stipulates that medical devices emitting radiations should be designed and manufactured in such a way that radiation exposures must be kept as low as reasonably acceptable for the intended purpose. Therefore, if tanning booths were considered equipment to overcome the deficit of vitamin D, they should not be equipped with UVA lamps and should only deliver UVB doses much weaker than now, just right for production of vitamin D. This would most likely lead to devices that would not induce a tan to users.

Chapters/sections: § 5.3- Efficacy of sunbed regulations, p22, lines 37-38

Comment: There are some indications that restrictions in sunbed use may succeed in reducing prevalence of use and, eventually, associated risks.

On the contrary, restrictions in sunbed use are not totally efficient. For example, despite a legal ban, minors have used sunbeds: 3.5 % of minors (15-17 years old) in France in 2010 [Baromètre cancer 2010] and 8.7 % of minors (14-17 years old) in Germany in 2012 [Diehl *et al.,* 2013]. Moreover, compared to adults, minors are more likely to use unsupervised sunbeds (in fitness center, swimming pool/sauna) and are less frequently advised by service personnel [Diehl *et al.,* 2013].

References:

Diehl *et al.* (2013). Use of sunbeds by minors despite a legal regulation: extent, characteristics, and reasons. J Public Health.

Beck F, Gautier A (dir.). Baromètre cancer 2010. Saint-Denis : Inpes, 2011.

Chapters/sections: § 7. Health effects, p34, lines 17-18

Comment: It should be noticed that there is also no consensus on whether increasing vitamin D level would be a desirable health intervention and there is no scientific evidence to support such an intervention. And even, if some interventions could be desirable for improving one's health in particular populations, these populations are not yet clearly identified nor the level below which such intervention would bring a health benefit.

Chapters/sections: § 7. Health effects, p44

Comment: On page 44 on the mechanisms underlying melanoma, it could be added that several *in vitro* studies have shown that melanocytes are more sensitive than keratinocytes to UVA in terms of induction of oxidative DNA damage and reduced DNA repair capacities (Wang et al. Proc. Natl. Acad. Sci. U. S. A., 2010, 107, 12180; Mouret et al. Photochem. Photobiol. Sci. 2012 11, 155–162). These results reinforce the conclusions made on the basis of animal studies of a melanin-driven oxidative pathway in melanoma.

Chapters/sections: § 7. Health effects, p42-44

Comment: Other animal models are used for the melanoma: pigs, dogs and horses.

Chapters/sections: § 7. Health effects, p 48, lines 41-43

Comment: The authors propose that, in animal studies, erythema can be used as a surrogate for cancer. This comparison may not be really relevant. Indeed, the two phenomena correspond to very different biological responses. In addition erythema is a short term process with a clear threshold, while cancer is a long term effect triggered by initial events (genotoxicity and mutagenesis) that do not exhibit a threshold response.

Chapters/sections: § 7. Health effects, p42, line 33 – *Experimental animal studies*

Comment: In the discussion of the mechanisms leading to non-melanoma skin cancers, the authors mostly describe UVA as an agent that induces oxidative DNA damage. This is true but a growing number of studies show that UVA also leads to the formation of cyclobutane pyrimidine dimers (Kielbassa *et al*., Carcinogenesis 1997; Perdiz *et al.* J. Biol. Chem. 2000; Douki *et al.* Biochemistry 2003; Mouret et al. Proc. Natl. Acad. Sci. USA 2006) and in larger amounts than oxidative damage. This observation is not only interesting from a photochemical point of view but also in terms of biological consequences. Indeed, cyclobutane pyrimidine dimers have been shown to be responsible for mutagenesis of UVB both *in vitro* and *in vivo* (You *et al.* J. Biol. Chem. 2001; Jans et al. Curr. Biol. 2005). Accordingly, the mutagenic signature of UVA in primary cell culture is very similar to that of UVB (Kappes et al. J. Invest. Dermatol. 2006, Ikehata et al. J. Invest. Dermatol. 2008). These recent results contrast with the early data cited by the report which were obtained in Chinese hamster ovary cells (Sage et al. Proc. Natl. Acad. Sci. USA 1996). The mutagenic effects of UVA are thus expected to be more important than previously believed.

Chapters/sections: § 7. Health effects, p42, line 38

Comment: On the mechanistic aspects, it may be added that UVA has been reported to decrease DNA repair capacities. Cyclobutane pyrimidine dimers are repaired more slowly in skin and in cultured cells when they are produced by UVA than by UVB (Courdavault et al. DNA repair 2005; Mouret et al. Proc. Natl. Acad. Sci. USA 2006). Moreover, exposure to a preliminary UVA dose decreases the repair rate of dimers in UVB irradiated keratinocytes (Courdavault et al. DNA repair 2005). A possible explanation could be the oxidation of repair protein (Montaner et al. EMBO Rep. 2007; Guven et al. J Invest Dermatol 2015). One can thus envision a double effect of UV radiation with UVB producing most of the DNA damage and UVA hampering their repair.

Chapters/sections: § 7. Health effects, p52, line 25

Comment: The authors refer to studies showing the formation of double-strand breaks in DNA as the result of exposure to UVA. Other researchers have shown that this is not a direct effect. This should be made clearer in order to prevent a wrong comparison between UVA and ionizing radiation.

Chapters/sections: § 7. Health effects, p57, line 40 - *ocular melanoma*

Comment: The authors mention several times in the text the role of UV in ocular melanoma. Nevertheless, the mechanistic link is not as strongly established than in the case of cutaneous melanoma, this point should be underlined.

Chapters/sections: § 8- Opinion, p60, lines 15-45 – Question 1

Comment: In addition to increasing skin cancer risk, immunosuppression and skin–aging, indoor tanning can cause acute and chronic eye diseases (if eye protection is not used), addiction, burns to the skin and, if tanning devices are not properly sanitized, skin infections.

To preserve the integrity of the genetic code, repair enzymes are activated almost immediately to correct the damage. In cells where extensive or irreparable injury occurs, these cells switch on the pathway for controlled self-destruction (apoptosis). Extensive data demonstrate that DNA damage or DNA repair intermediates are powerful signals that initiate melanogenesis. Tanning is a biological signal by the skin that reflects the presence of DNA impairment.

Chapters/sections: § 8- Opinion, p61, lines 12-16 – Question 2

Comment: We propose that some elements discussed in the abstract or the main report may be added in the response:

From the Abstract, Overall conclusion: "The SCENIHR concludes that UV is a complete carcinogen, both an initiator, and a promoter. There is strong evidence that sunbed exposure causes skin melanoma, squamous cell carcinoma and, to a lesser extent, basal cell carcinoma, more especially when first exposure takes place in younger ages. There is moderate evidence that sunbed exposure may also cause ocular melanoma. Sunbed use is responsible for a noticeable proportion of both melanoma and non-melanoma skin cancers and for a large fraction of melanomas arising before the age of 30."

Because of evidence of the carcinogenic effects of artificial UV exposure and of the nature of skin cancer induction, we agree that there is no safe limit for UV irradiance from UV lamps, especially sunbeds. So, no threshold levels of UV-irradiance and UV–dose can be specified for the protection of the health and the safety of users.

"The UV emission of a modern tanning appliance corresponds to an UV index of 12, i.e. equivalent to midday tropical sun." (cf. § 6.2 UV exposure from sunbeds –trends in UV irradiance, page 26). In this case, the level of protection is not sufficient to ensure the health and safety of users. By setting sunbeds to a high UV index (usually 12 equivalent to midday tropical sun), it is expected to reach maximal UV damage.

Unlike sun exposure, indoor tanning provides concentrated UV exposure regardless of geographical location, time of year, or time of day. Indoor tanning also exposes areas of the body not normally exposed to intense UV radiation, further increasing risk. Indoor tanning should therefore be completely avoided. Prevention messages should aim to that goal in addition to those used to reduce sun exposure.

Chapters/sections: § 8- Opinion, p61, lines 23-29 – Question 3

Comment: The authors discussed the minimal irradiance and wavelength mostly in terms of UVC radiation. The latter wavelength range may not be the most relevant. UVC is readily absorbed by the DNA of cultured cells and induces numerous damage and mutations. However, the situation is different in full skin. Indeed, the stratum cornea absorbs most of the UVC which reaches the nucleated cells of the epidermis only in minute amount. The minimal wavelengths to consider are more likely the most energetic UVB.

Chapters/sections: § 8- Opinion, p61, lines 31-32 – Question 3

Comment: All wavelength of UV are dangerous. Ultraviolet radiations (bandwidth 100–400 nm, encompassing UVC, UVB and UVA) are carcinogenic to humans according to the IARC. UV radiations are a complete carcinogen, both an initiator, and a promoter. So, there is no safe limit for UV irradiance from UV lamps.

Chapters/sections: § 9- Recommendation for further work

Comment: The French Agency for Food, Environmental and Occupational Health & Safety (Anses) and the French Institute for Public Health Surveillance (InVS) totally agree with the Scenihr conclusions. The document is well documented and provides very strong conclusions. The overall document presents an exhaustive up-to-date evaluation of the scientific knowledge both from human and animal studies on the potential risks from sunbed use.

Anses and InVS propose to add a recommendation for further reflexing on regulation:

In a context of rapid expansion of the marketing and use for cosmetic purposes of radiation-emitting devices with a proven carcinogenic effect, and moreover without any beneficial effect on health, associated with the reduced effectiveness of the regulation to ensure protection for the health and safety users of tanning device, ANSES believes that the European regulation constitutes only a partial and insufficient response in light of the proven risk of skin cancer for their users.

Indeed, regulations governing the methods of public access to tanning devices for cosmetic purposes are unable to prevent the health impact of artificial UV rays. Given the health data already presented, it would be preferable for the authorities to alert the European Commission concerning the safety of use of tanning devices.

Since 2012, ANSES therefore recommends the cessation, ultimately, of all commercial use of tanning by artificial UV rays and of the sale of appliances emitting artificial UV rays for cosmetic purposes (see OPINION of the French Agency for Food, Environmental and Occupational Health & Safety relating to a draft decree concerning the sale and provision to the public of certain tanning devices that use ultraviolet radiation available online in English: https://www.anses.fr/en/system/files/AP2012sa0263EN.pdf).