The Director General

Maisons-Alfort, 30 July 2018

OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

on exposure to artificial ultraviolet radiation emitted by sunbeds

ANSES undertakes independent and pluralistic scientific expert assessments.
ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.
It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with the necessary information concerning these risks as well as the requisite expertise and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are published on its website. This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 30 July 2018 shall prevail.

On 17 May 2018, the Directorate General for Health (DGS) made a formal request to the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), the National Cancer Institute (INCa) and the French Public Health Agency (ANSP) to update the health data on artificial tanning and, regarding ANSES more specifically, to provide a summarised update of its expert appraisals on the health effects of exposure to artificial ultraviolet radiation.

1. BACKGROUND AND PURPOSE OF THE REQUEST

In May 2005, the French Agency for Environmental Health (AFSSE) issued an opinion along with an expert appraisal report on the risks of exposure to natural and artificial ultraviolet (UV) radiation. Since then, ANSES has published opinions based on advances in the available scientific knowledge on the hazards associated with the use of sunbeds, and specifically the following:

- 2012: Opinion on a draft decree on the sale and public provision of certain devices using ultraviolet radiation;
- 2014: Opinion issued during the consultation on two draft orders implementing the above-mentioned Decree No. 2013-1261;

In addition, in 2017, ANSES prepared a summary note during the public consultation for the draft report "Opinion on Biological effects of ultraviolet radiation relevant to health with particular reference to sunbeds for cosmetic purposes" produced by the European Commission's Scientific Committee on Health, the Environment and Emerging Risks (SCHEER).

Article 24 of Decree No. 2013-1261 of 27 December 2013 on the sale and public provision of certain devices using ultraviolet radiation stipulates that: "At the end of a four-year period beginning on 1 January 2014, a report by the Ministers of Health and Consumer Affairs will assess the conditions under which these regulations are applied and the health consequences of exposure to artificial ultraviolet radiation".

On 17 May 2018, the DGS made a formal request to ANSES, INCa and the ANSP to gather the scientific information needed to prepare this report.

2. ORGANISATION OF THE WORK

This opinion falls within the sphere of competence of the Expert Committee (CES) on "Assessment of the risks related to physical agents, new technologies and development areas". It was consulted on this work on 19 June 2018.

As the formal request was sent jointly to ANSES, INCa and the ANSP, ANSES regularly communicated with the other two bodies consulted by the DGS in order to identify the specific questions addressed to each agency.

With regard to ANSES's contribution, expert rapporteurs were appointed to carry out a critical analysis of the expert assessments by international organisations and the most recent publications on the health risks associated with exposure to artificial UV radiation. In view of the deadline imposed for the Agency's response, this review was carried out not through systematic questioning, but on the basis of the knowledge of the experts involved and any comments provided by the CES consulted.

ANSES analyses interests declared by experts before they are appointed and throughout their work in order to prevent risks of conflicts of interest in relation to the points addressed in expert appraisals. The experts' declarations of interests are made public via the ANSES website (www.anses.fr).

The expert appraisal was carried out in accordance with French Standard NF X 50-110 "Quality in Expert Appraisals– General Requirements of Competence for Expert Appraisals (May 2003)".

3. SUMMARY AND ANALYSIS OF THE SCIENTIFIC DATA

■ Summary of previous work by the Agency and international organisations

Since 1997, when the first decree regulating the use of tanning devices in France was published (proportion of UVB[1] radiation limited to 1.5% of total irradiance, prohibition for minors, requirement to train professionals and inform the public), several organisations, including ANSES (see Table 1), have published scientific reports and/or issued opinions on the health risks of indoor tanning.

As early as 2005, AFSSE, in a joint report with the French Institute for Public Health Surveillance (InVS) and the French Health Products Safety Agency (AFSSAPS), mentioned the recent discovery of the mutagenicity of UVA radiation. An analysis of the scientific studies showed a positive association between exposure to tanning devices and the risk of melanoma (OR = 1.25 [1.05-1.49]), with this risk being further increased by early ("first exposure as a young adult"; OR = 1.7 [1.3-2.2]) or frequent ("longer duration or higher frequency of exposure" OR = 1.6 [1.2-2.1]) exposure. Consequently, AFSSE recommended avoiding exposure to artificial UV radiation.

In response to a request from the French Ministry of Health, the International Agency for Research on Cancer (IARC) convened a working group in June 2005 to assess the health effects, and more specifically the carcinogenicity, of exposure to artificial tanning. The IARC produced a meta-analysis of 19 studies showing that the use of artificial tanning is associated with a risk of melanoma (RR = 1.15 [1.00-1.31]), and that the risk is increased when exposure begins before the age of 30 (RR = 1.75 [1.35-2.26]). For non-melanoma skin cancers, it has been shown that the use of artificial tanning is associated with an increase in the risk of squamous cell cancer (3

[1] Ultraviolet radiation is usually classified into three wavelength ranges, their precise limits having been arbitrarily determined: UVA (315-400 nm), UVB (280-315 nm) and UVC (100-280 nm).

studies: RR = 2.25 [1.08-4.70]), but not in the risk of basal cell cancer (4 studies: RR = 1.03 [0.56-1.90]) (IARC, 2006).

In 2006, the European Commission's Scientific Committee on Consumer Products (SCCP[2]) issued an opinion stating that the use of UV-emitting tanning devices may increase the risk of skin melanoma and possibly ocular melanoma. The SCCP added that the use of tanning devices should be discouraged for people with known risk factors (skin phototypes I and II[3] and presence of freckles[4], atypical and/or multiple moles, family history of melanoma). Since the risk of melanoma appears particularly high when tanning devices are used at an early age, tanning devices should not be used by people under 18 years of age. In addition, the SCCP suggested that the maximum erythemally-weighted irradiance of these devices should not exceed 0.3 W/m^2, or 11 standard erythema doses (SED[5]) per hour, or a UV index of 12, equivalent to exposure to tropical sunlight, which the World Health Organisation (WHO) considers extreme.

In 2009, the IARC re-assessed the epidemiological, experimental and biological data on exposure to artificial UV radiation from sunbeds. Based on the results of two meta-analyses, the one conducted by the IARC in 2006 (IARC, 2006) and a new meta-analysis (Hirst *et al*., 2009) including a new case-control study nested in a cohort (Han *et al.,* 2006), and also on new biological data showing the ability of UVA radiation to induce C-to-T mutations of the same type as those previously considered specific to UVB or C radiation, the IARC classified exposure to UV radiation emitted by sunbeds as carcinogenic to humans (Group 1) (IARC, 2012).

In November 2009, the DGS asked INCa to review the current state of knowledge on cancer risks in France associated with artificial-tanning facilities and to make the necessary recommendations to prevent these risks for users. Coming shortly after the IARC's classification, the INCa working group confirmed the IARC's analyses and was also able to draw on updated data on the Scandinavian cohort and a published analysis of a melanoma epidemic in Iceland (see details below). In conclusion, INCa stated that "recent epidemiological data affirm the existence of a relationship between melanoma risk and exposure to artificial UV... [in particular] when the first exposure occurs at an early age, before 35 years of age. In view of the epidemiological results, in particular the study by Veierød *et al*. (2010) and the study by Han *et al*. (2006), it is not possible to conclude as to the number of sessions below which there would be no risk of melanoma". In addition, INCa noted that exposure to artificial UVs could have a promoting effect on melanoma risk.

In 2012, researchers from the International Prevention Research Institute, the InVS, the National Institute for Prevention and Health Education (INPES), INCa, and the Cancer Research Centre in Lyon joined forces to quantify the impact of artificial UV exposure on the incidence and mortality of skin melanomas in France. The attributable fraction was estimated from exposure prevalence data produced by the 2010 Cancer Barometer and from the relative risk of the IARC's meta-analysis (IARC, 2006). It appears that for 2008, 4.6% of skin melanoma cases (347 annual cases) were attributable to the use of sunbeds, with women being the most likely to support this risk, as they accounted for about 76% of cases. Different alternative scenarios led to the assessment that each year, between 91 and 350 cases of melanoma are due to the use of sunbeds. Assuming that cases induced by sunbeds have the same prognosis as those induced by natural UV radiation, between 19 and 76 deaths per year can be attributed to this practice. Between 566 and

[2] Now known as the Scientific Committee on Consumer Safety (SCCS)

[3] Skin phototypes; skin's reaction to the first exposure to the sun. Sensitive phototypes I and II always burn and do not tan or only tan a little. Phototypes III burn and tan moderately, phototypes IV rarely burn and tan well.

[4] Pigmented skin spots

[5] 1 SED = 100 J/m^2

2288 deaths can be expected in the next 30 years if French population exposure to UV booths does not change (Boniol *et al.*, 2012a).

A new analysis of a Scandinavian cohort, after an average follow-up period of 14 years, focused on 106,366 women, representing a cohort of 1,489,298 person-years and 412 cases of melanoma. This study found, in a stratified analysis by age category, a significant association between the increase in relative risk of melanoma and exposure to artificial UV radiation at least once a month at an age between 10 and 39 years. The relative risk was 1.38 ($CI_{95\%}$ [0.98-1.94]) when women were exposed in one of the three periods 10-19 years, 20-29 years or 30-39 years, while it was 2.37 ($CI_{95\%}$ [1.37-4.08]) when women were exposed in two or three periods 10-19 years, 20-29 years or 30-39 years (Veierød *et al.,* 2010). These results suggest an increase in risk with an increase in exposure time.

In November 2012, the DGS sought an Opinion from ANSES on a draft decree designed to amend the Decree of 30 May 1997 on the sale and public provision of certain tanning devices using ultraviolet radiation. In its opinion (ANSES, 2012), ANSES drew firstly on the IARC's classification of UV radiation emitted by sunbeds as "Carcinogenic to humans" (Group 1) and secondly on the following major studies, which were subsequent to the IARC's classification:

- A population case-control study including 1167 cases and 1101 controls aged 25 to 59 years showed an adjusted risk of 1.74 (1.42-2.14) for exposure at least once (Lazovich *et al.,* 2010). This study also showed a significant dose-response relationship, both for the number of annual sessions and for the number of years of use. Among the many significant results of this study, it is worth noting a doubling of the risk of sunburn in the case group (OR = 2.00 [1.48-2.70]), suggesting that artificial tanning does not protect against the effects of the sun, and that the risk was greater with the use of more powerful devices, or primarily UVA-emitting or UVB-enhanced devices.

- Another analysis in the same study, excluding people who had suffered from burns when using artificial tanning, examined the relationship between the use of artificial tanning and the risk of melanoma based on the number of sunburns received from outdoor sun exposure over a lifetime, divided into four classes; 0, 1-2, 3-5, >5 (Vogel et al., 2014). A significant increase in the melanoma risk was found in tanning booth users for all categories of sunburn. The highest risk of melanoma was found for tanning booth users who had never suffered from sunburn (OR = 3.87 [1.68-8.91]). These results show that indoor tanning is a risk factor for melanoma, even in individuals who have never had sunburn outdoors.

- In Australia, a population-based case-control study examined 604 melanoma cases diagnosed between the ages of 18-39 years, and 479 controls (Cust *et al.*, 2011). The risk of melanoma associated with exposure at least once to indoor tanning was 1.41 [1.01-1.96]), and was 2.01 [1.23-3.31]) for a total of more than 10 sessions. The association was stronger when first exposure occurred at less than 25 years of age (OR = 1.64 [1.07-2.51]) and for melanomas diagnosed in younger people: OR for more than 10 sessions = 6.57 [1.41-30.49] for melanomas diagnosed between 18 and 29 years of age. For cases where the individuals had used indoor tanning and the melanoma had been diagnosed between the ages of 18 and 29, 76% of the melanomas were attributable to the use of indoor tanning.

- Iceland is a Nordic country that has been experiencing a melanoma epidemic since 1995. While before 1995 the incidence of melanoma in Iceland was lower than in Denmark or

Sweden, this incidence increased sharply to exceed that of the other Nordic countries around 2000. The phenomenon was particularly pronounced for the incidence of trunk melanomas in women under 50 years of age; between 1995 and 2002, this incidence increased by 20.4% per year, resembling an epidemic incidence curve, and in 2002, it was higher than the incidence of melanomas on the lower limbs. The only plausible explanation for this epidemic was the massive exposure of young Icelanders to artificial-tanning devices after 1985, with the hypothesis of UV exposure during trips abroad having been ruled out. In 1979, there were only three tanning salons in Reykjavik, while in 1988, 56 salons and 207 devices were in use. Exposure to tanning devices in Iceland increased rapidly after 1985, mainly among young women, and in 2002, 70% of women and 35% of men in Iceland had used a tanning device at least once (Rafnsson *et al.,* 2004). Héry *et al.* (2010) therefore suggested that the high prevalence of tanning device use had probably contributed to the sharp increase in melanoma incidence in Iceland. As this increase in incidence was not accompanied by an increase in mortality, it is likely that it concerned a non-metastatic form of melanoma.

- To update the IARC's meta-analysis (2006), Boniol *et al*. (2012b) conducted a new meta-analysis of the melanoma risk associated with exposure to tanning devices, including 27 studies. The increased risk associated with using UV booths (once or more) was 20% (meta RR = 1.20 [1.08-1.34]), with a higher risk when the first use was before 35 years of age (meta RR of 1.59 [1.36-1.85]). This meta-analysis also showed a dose-dependent effect: a 1.8% increase (0-3.8) for each annual exposure session.

In its conclusion, ANSES considered that the draft decree constituted a partial and insufficient response in light of the proven risk of skin cancer for users, and recommended that all commercial use of artificial UV tanning and sale of devices delivering artificial UVs for cosmetic purposes should eventually be stopped.

The meta-analysis by Colantonio *et al.* (2014) was published subsequent to ANSES's opinion, reinforcing the results of Boniol *et al.* (2012b). Colantonio *et al.* (2014) conducted a meta-analysis of the melanoma risk associated with exposure to tanning devices, including 31 studies. The risk associated with exposure at least once was 1.16 (1.05-1.28). A similar result was obtained for the recent studies (recruitment in 2000 and after): OR = 1.22 [1.03-1.45], suggesting that recent devices are no "safer" than older ones. This meta-analysis also suggested a dose-response relationship: use for a duration of 1 year or less is associated with an OR of 1.37 [1.06-1.77], while use for more than 1 year is associated with an OR of 1.61 [0.98-267], and more than 10 tanning sessions over a lifetime results in a 34% increased risk (OR = 1.34 [1.05-1.71]).

In late 2016, the SCHEER[6] published an opinion on the biological effects of UV radiation, with particular reference to sunbeds (SCHEER, 2016). This opinion, based on new data published since the SCCP (2006) opinion, concluded that case-control and cohort epidemiological studies provide strong evidence of the significant increase in melanoma risk associated with the use of tanning devices, particularly at an early age. The SCHEER further estimated that in Europe, 3438 (5.4%) of the 63,942 new melanoma cases each year were attributable to the use of tanning devices for all ages, and that 43% of melanoma cases in young subjects in France and 76% in Australia could be attributed to exposure before the age of 30. With regard to non-melanoma skin cancers, the SCHEER stated that there is strong evidence that the use of tanning devices is also a risk factor for squamous cell and, to a lesser extent, basal cell cancers, particularly when exposure occurs at an early age. The SCHEER also stated that no irradiance or dose limit can

[6] The European Commission's Scientific Committee on Health, Environmental and Emerging Risks

be given to ensure the protection of tanning device users, due to the evidence of the carcinogenic effect of UV radiation from tanning devices and the stochastic nature of skin cancer induction.

Since the SCHEER opinion was published, two new epidemiological studies have confirmed the level of evidence: a new analysis of a major case-control study in the United States (Lazovich *et al.*, 2016) and a Norwegian cohort study (Ghiasvand *et al*., 2017).

In the United States, Lazovich *et al*. (2016) re-analysed data from a population-based case-control study (681 cases aged 25 to 49 years, diagnosed between 2004 and 2007, and 654 controls) to examine the association between indoor tanning and melanoma in people under 50 years of age. The results show that women under 40 years of age started tanning sessions earlier than women aged 40-49 years (16 *vs* 25 years, $p < 0.0001$), and reported more frequent artificial tanning (median number of sessions: 100 *vs* 40, $p < 0001$). The melanoma risk associated with indoor tanning was increased in women of all age groups: OR_{crude} = 6.0 [1.3-28.5] for women under 30 years of age, $OR_{adjusted}$ = 3.5 [1.2-9.7] for women aged 30-39 years, $OR_{adjusted}$ = 2.3 [1.4-3.6] for women aged 40-49 years; with a dose effect regardless of age. For men, the age-specific results were inconsistent. The highest risk per anatomical site was observed for trunk melanomas in women: $OR_{adjusted}$ = 3.7 [1.9 – 7.2].

Ghiasvand *et al*. (2017) studied the risk of melanoma associated with exposure to tanning devices in a cohort of 141,045 Norwegian women, aged 34 to 64 years at inclusion, followed for 13.7 years (1,930,583 person-years), and in which 861 melanomas appeared. The results show that the risk of melanoma increases with the cumulative number of tanning sessions (adjusted RR = 1.32 [1.08-1.63] for the highest tertile compared to no exposure). Starting tanning sessions before the age of 30 is associated with an adjusted RR of 1.31 [1.07-1.59] compared to no exposure. Most importantly, women who started tanning sessions before the age of 30 were on average 2.2 years [0.9-3.4] younger at diagnosis than women who had never used artificial tanning. As noted in a commentary accompanying the publication of this work, the latter result supports a promoting effect of UV exposure from sunbeds (Berwick and Doré, 2017).

All these data are summarised in the WHO document "Artificial tanning devices" (2017), which states in particular: "the adverse health effects associated with sunbed use are now well documented and the body of evidence continues to grow. Cancer, sunburns, accelerated skin ageing, eye inflammation and transient immunosuppression are all associated with sunbed use. Of these, cancer is by far the most serious [...]"[7].

Reichrath *et al*. (2018) questioned the recent opinions by the SCHEER (2016) and the WHO (2017) which, in their view, did not adequately take into account the positive and negative effects of exposure to tanning devices, particularly the many benefits of vitamin D production. However, numerous controlled vitamin D supplementation trials have so far been unable to demonstrate their efficacy on most non-skeletal disorders (cardiovascular disease, mood disorders, etc.) (Autier *et al.*, 2017).

Burgard *et al*. (2018) conducted a new meta-analysis of the risk of melanoma associated with indoor tanning. The results of this new meta-analysis are similar to those of the meta-analyses by Boniol *et al*. (2012b) and Colantonio *et al*. (2014), but the authors' interpretation of these results is different. The authors assessed the quality of the studies using the Newcastle-Ottawa Quality Assessment Scale, known to yield arbitrary results (Stang, 2010). They concluded that the observational studies generally seem to be of poor quality and biased, so that the increased risk

[7] Artificial tanning devices - Public health interventions to manage sunbeds - WHO - 2017, p.11.

of melanoma associated with indoor tanning may be a fallacious result. In addition, it is regrettable that their literature search stopped in January 2016 and did not allow two studies confirming the influence of age at first exposure to be taken into account (Lazovich *et al.*, 2016, Ghiasvand *et al*., 2017). Lastly, it should be noted that some of these authors report receiving funding from foundations connected to the tanning industry.

A recent calculation (Arnold *et al*., 2018) estimated that in France in 2015, in adults over 30 years of age, 10,340 cases of melanoma (83% of melanomas and 3% of all cancers) could be attributed to sun exposure, and 382 cases of melanoma could be attributed to exposure to tanning devices (1.5% of melanoma cases in men and 4.6% in women).

Table: 1 Summary of ANSES's expert appraisal work since 2004

Request				Response		
Requested by	Received by	Date	Purpose of the request	Date	Format	Conclusions/messages about artificial UV
DGS/DGPR	AFSSE InVS AFSSAPS	06/09/2004	Review of current knowledge on exposure and the health risks.	23/05/2005	AFSSE opinion	ANSES formally advises against the use of UV tanning devices. In addition, the expert group wishes to maintain the classification of UV-emitting tanning devices as set out in Standard NF-EN-60335-2-27, 4th edition, 2000.
			InVS: characterise the exposure of the French population. AFSSAPS: "ultraviolet radiation and use of cosmetic products".	June 2005	Joint AFSSE/AFSSAPS/InVS report	
DGS	INCa	13/11/2009	Carry out a review of knowledge on cancer risks in France associated with artificial-tanning facilities (April 2010).	April 2010	Report	The practice of artificial UV tanning is strongly discouraged. Exposure to artificial UV radiation has no health benefits: - it does not prepare the skin for the sun; - it contributes very little or not at all to the production of vitamin D; - it causes premature skin ageing. The regulatory framework for practices only aims to reduce as far as possible the damage caused in the short and long term.
			Following the contribution of ANSES and InVS to INCa's work, the two agencies drafted a joint note to the DGS.	07/09/2010	Joint ANSES/InVS note	Alert on the alarming nature of the health risks associated with this practice. Recommendation to cease all commercial use of artificial UV tanning and sale of equipment.
DGS	ANSES	29/11/2012	ANSES Opinion on a draft decree designed to amend the Decree of 30 May 1997 on the sale and public provision of certain tanning devices using ultraviolet (UV) radiation (following the Opinion of 31 May 2012, consultation run from 29 November to 19 December 2012).	19/12/2012	Opinion	Proposed amendments to certain articles of the Decree. + "ANSES considers that the draft decree constitutes a partial and insufficient response in light of the proven risk of skin cancer for their users"; + "ANSES therefore recommends that all commercial use of artificial UV tanning and sale of devices delivering artificial UVs for cosmetic purposes should eventually be stopped"; + "ANSES wishes to draw the attention of the European Commission to the safety of use of tanning devices".

Request				Response		
Requested by	Received by	Date	Purpose of the request	Date	Format	Conclusions/messages about artificial UV
DGS	ANSES	20/06/2014	ANSES Opinion on two draft orders implementing Decree No. 2013-1261 of 27/12/2013 on the sale and public provision of certain tanning devices using ultraviolet radiation.	03/07/2014	Opinion	Proposed amendments to certain articles of the orders. + "ANSES considers that Decree No. 2013-1261 and its implementing orders constitute a partial and insufficient response in light of the proven risk of skin cancer for their users"; + "Action 12.8 of the 2013-2019 Cancer Plan stipulates that the authorities should draw the attention of the European Commission to the safety of use of tanning devices with a view to changing the European regulations"; + "ANSES therefore recommends that all commercial use of artificial UV tanning and sale of devices delivering artificial UVs for cosmetic purposes should eventually be stopped".
DGS	ANSES	14/03/2016	1) Analyse the draft opinion and respond to the SCENIHR consultation 2) Summarise the SCENIHR's draft opinion 3) Update the latest ANSES opinion on tanning devices in light of any new scientific evidence provided by the SCENIHR's final opinion	20/04/2016	Response to the public consultation	ANSES responded to the public consultation.
				17/05/2016	Summary of the draft opinion of the SCHEER[8]	ANSES considers that the SCHEER's opinion is well documented.
				04/04/2017	DGS letter	"It does not seem appropriate to update the latest opinion published by ANSES, as the recommendations remain valid".

[8] The SCHEER (Scientific Committee on Health, Environmental and Emerging Risks), replaced the SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks) in 2016.

Sunbeds: very intense exposure, especially to UVA radiation

To understand the harmful effects of solar radiation, it is common practice in the first analysis to distinguish the respective roles of UVBs, which have the most energy but are also the least prevalent (less than 5% of the solar UV spectrum), and UVAs, which are less energetic but account for more than 95% of solar UVs.

Decree No. 2013-1261 of 27 December 2013 sets an upper limit for the total UV intensity emitted by tanning devices, which corresponds to a UV index[9] of 12. The latter value is particularly high, with UV indices in France being around 8 or 9 at most (http://www.meteofrance.fr/prevoir-le-temps/meteo-et-sante/les-ultraviolets). Artificial-tanning devices therefore provide exposure to intense sources that are, moreover, much higher in UVA than natural light. This high UVA prevalence must be taken into account in the photobiological consequences of exposure to tanning devices. Thus, it has been estimated that while only 20 to 30% of the erythemal dose of natural sunlight is due to UVA radiation (Sola *et al.,* 2015), this proportion can increase to 80% with tanning devices. The authors draw the same conclusion for photoageing, which may be four times faster with tanning lamps than with the sun (see below).

Carcinogenic and genotoxic effect of UVAs

While the carcinogenicity of UVBs has been known for decades, UVA radiation has long been considered relatively harmless, certainly because it has less capacity to cause erythema. Decree No. 97-617 of 30 May 1997 limited the irradiance related solely to UVBs to 1.5% of the total UV irradiance emitted by artificial-tanning devices.

In 2012, the IARC classified exposure to solar UV radiation and UV-emitting tanning devices as carcinogenic to humans (Group 1) (IARC, 2006). For UVAs, this classification was based in particular on animal experiments showing the induction of skin cancer (de Laat *et al.*, 1997) or the pro-metastasic nature of UVAs (Pastila *et al.*, 2005). More recent studies have further investigated the biological mechanisms and have shown, for example, the involvement of melanin in melanomas induced by UVAs (Noonan *et al.*, 2012). These results are in agreement with data showing that although melanin is an excellent shield against UV radiation, it has oxidative power when it absorbs UVA.

From a molecular point of view, it is now well established that DNA damage induced mainly by UVAs is of the same type as that induced by UVBs (Mouret *et al.*, 2006; Tewari *et al.*, 2013), but with lower effectiveness. Specific mutations of this damage have been found after exposure to UVAs (Ikehata *et al.*, 2008; Rünger, 2008). Lastly, more recent studies have shown that by oxidising the proteins involved in DNA repair (Karran *et al.*, 2016), UVAs reduce the DNA repair capacities of cells, both in keratinocytes, which are responsible for carcinomas (Courdavault *et al.*, 2005), and in melanocytes, which are responsible for melanomas (Kimeswenger *et al.,* 2018). Moreover, the skin colouring induced by UVAs, which is a melanin oxidation reaction but not *de novo* production as in natural tanning, has been shown to provide no protection against the formation of DNA damage induced by UVB exposure (Coelho *et al.*, 2014).

Other health effects

- Addiction to indoor tanning

While the motivation for using artificial tanning is essentially aesthetic, some recent results suggest that frequent or excessive use of tanning devices could be regarded as addictive behaviour (Kourosh *et al*., 2010; Petit *et al*., 2014; Reed *et al*., 2016; SCHEER, 2016). Studies in

[9] The UV index reflects solar UV exposure and the hazards for health. It is calculated from the spectrum of sunlight on the ground according to the following formula: UV index = integral according to the wavelength of the power (watt/m²/wavelength unit) × 40 (in m²/W) × erythema action index (1 for wavelengths below 300 nm, 0.1 for 310 nm, 0.01 for 320 nm and 0.001 for 330 nm).

students have indicated that, among participants who had used indoor tanning, 5 to 30% of them met the criteria for an indoor-tanning addiction or tanning dependence (Mosher and Danoff-Burg, 2010; Hillhouse *et al*., 2012; Ashrafioun and Bonar, 2014). More recently, Cartmel *et al*. (2017) and Stapleton *et al*. (2017) confirmed the existence of this dependence in some users and indicated the need to consider and treat it.

However, the mechanism of this dependence or addiction is not currently known. It could involve a "reward" response. In support of this hypothesis, Aubert *et al*. (2016) used a single-photon emission computerised tomography (SPECT) technique to show an increase in dopamine flow during exposure to a tanning device in ten individuals using UV booths addictively, but not in a comparable sample of occasional users.

- Immunosuppression

UVA and UVB radiation cause local and systemic immunosuppression, which can result in a decrease in the elimination of precancerous lesions. It is now clear that UVA- and UVB-induced immunosuppression plays a role in the progression of skin cancer (Schwarz *et al.*, 2010). This mechanism may explain the melanoma-promoting action of artificial UV radiation revealed in some epidemiological studies (Lazovich *et al.*, 2016; Ghiasvand *et al.*, 2017).

In the UVB region, immunosuppression peaks at 300 nm, and at 370 nm in the UVA region (Damian *et al.*, 2011). Given the proportion of UVAs and UVBs in solar radiation, the involvement of UVAs in sun-induced immunosuppression can be estimated at 60%. This proportion is far higher with solar lamps, which are low in UVBs. It should also be noted that UVA radiation has the ability to reduce immunosuppression due to UVBs (Garssen *et al.*, 2001; Reeve *et al.*, 1998). However, since the UVB/UVA ratio is not the same in tanning lamps as with sunlight, it cannot be automatically assumed that this phenomenon occurs during exposure to artificial UV radiation.

Studies in animal models have suggested that UV exposure alters the effectiveness of immunisation and reduces vaccine-induced resistance (Byrne *et al*., 2006; Norval and Halliday, 2011). In humans, sun exposure can reduce the efficacy of viral vaccines (poliovirus, influenza, hepatitis B, rubella) administered in tropical areas or in summer (Norval and Halliday, 2011 for review), and protection against tuberculosis decreases with proximity to the equator (Colditz *et al.*, 1994). Few data are available on the effect of artificial UV exposure on vaccine efficacy (De Gruijl, 2008).

- Photoageing

Sunbeds are mainly used for cosmetic reasons. Paradoxically, UV exposure is a major cause of accelerated skin ageing. The biological bases of this process are well known (Fisher *et al.,* 1997) and implicate UVA radiation in particular (Battie *et al.,* 2014). Recent *in vitro* data have confirmed the role of oxidative stress (Yoshimoto *et al.,* 2018) and metalloproteinase production (Nakyai *et al.*, 2017; Zheng *et al.,* 2018), especially after repeated exposure of fibroblasts in culture. These mechanisms lead to protein degradation in the extracellular matrix of the dermis and the loss of the skin tissue's mechanical properties. The important role played by UVAs in photoageing means that this process is estimated to occur four times faster after exposure to sunbeds than to natural light (Sola *et al.,* 2015).

No beneficial effects

- Artificial-tanning lamps and vitamin D

It is true that exposure to tanning devices can produce vitamin D (Weber, 2017; Kimball *et al.,* 2017). However, vitamin D production is a phenomenon almost exclusively due to UVB radiation.

As this part of the UV spectrum is limited to 1.5% of total UV irradiance, significant vitamin D production via tanning devices would therefore require a considerable prolongation of exposure.

In addition, a study exposing volunteers to simulated sunlight showed that the concentration of 25(OH)vitamin D rapidly exceeded the deficiency threshold to reach a plateau slightly below the concentration considered optimal (Rhodes *et al.,* 2010). The appearance of this plateau can be explained by photoreactions of vitamin D degradation. A recent theoretical study showed the importance of taking these photodegradation processes into account in models to explain the experimental data on vitamin D formation (Van Dijk *et al*., 2016).

In addition, recent data show that exposing the skin of the face and hands to the sun in summer, for 20 and 15 minutes in Lille and Manchester respectively, leads to a 25(OH)vitamin D serum concentration well above the deficiency threshold (C. Broniez, personal communication; Rhodes *et al.,* 2010). These low exposure levels are only accompanied by a slight induction of DNA damage that is quickly repaired (Felton *et al.*, 2016).

The use of sunbeds does not therefore provide a significant amount of vitamin D, which moreover is largely provided by reasonable and short-duration exposure to natural sunlight.

- "Preparation" of the skin for tanning

Tanning, which results from the synthesis of melanin by melanocytes in the basal layer of the epidermis and its transfer to the keratinocytes in the upper layers of skin, is essentially a reaction triggered by UVB radiation. UVA-induced skin colouring, which is not tanning, results from a melanin oxidation reaction and a redistribution of the pigment, but not from *de novo* production as in natural tanning. It therefore provides no protection against the formation of DNA damage induced by UVB exposure (Coelho *et al.*, 2014).

This means that exposure to artificial UV radiation does not prepare the skin for sun exposure and does not protect against sunburn (Lazovich *et al.,* 2010).

- **Public health effectiveness of regulations on tanning devices in different countries**

Some studies suggest that restrictions on the use of tanning devices may have the effect of reducing the prevalence of use and, potentially, the associated risks (SCHEER, 2016).

In the United States, the prevalence of teenage indoor tanning use in the previous year varied little between 1998 and 2004 (10 to 11%). In states that adopted regulations on minors' access to sunbeds, prevalence remained the same or decreased from 1998 to 2004, while it increased in states that did not adopt such regulations. However, these trends were not significant (Cokkinides *et al.,* 2009). Analysis of data from the national "Youth Risk Behavior" surveys conducted in 2009 and 2011 on 31,835 people suggested that tanning booth regulations, and in particular those with age-specific access restrictions, can reduce the prevalence of indoor tanning among young female high-school students, who have the highest use rates. Use of sunbeds is lower in states with age restrictions or parental consent requirements than in states without any regulations. No significant effects were observed in boys (Guy *et al*., 2014).

The most convincing data come from Iceland, where the high prevalence of indoor tanning has probably contributed to a sharp increase in melanomas since 1995. The campaign initiated by the Icelandic health authorities in the late 1990s probably led to a decrease in the incidence of trunk melanoma in women after 2002. A new campaign by the health authorities in 2004 to discourage the use of tanning devices, particularly by adolescent girls, resulted in a 50% reduction in tanning devices in 2008 (Héry *et al*., 2010).

A recent study (Pil *et al.,* 2016) analysed the current and future economic burden of skin cancers in Belgium, estimating that the incidence is likely to triple in the next twenty years, and attempted to assess the cost-effectiveness of primary prevention. The total economic burden of skin cancers in Belgium for 2014 was estimated at 106 million euros, with a cumulative cost of 3 billion euros by 2034; 65% of this cost being due to melanoma. It has been estimated that over a 50-year period, an awareness campaign and a total ban on the use of tanning devices would lead to a gain in life-years (QALY - quality-adjusted life-years) and budget savings: for every euro invested in the campaign, €3.6 would be saved in the long term for the funding of the health system.

4. AGENCY CONCLUSIONS AND RECOMMENDATIONS

In 1997, the first decree regulating the use of tanning devices in France was published. This decree included a number of provisions, including a limitation of the proportion of UVBs to 1.5% of total irradiance, in line with the state of knowledge on the risks associated with exposure to this range of UV radiation.

In 2009, the International Agency for Research on Cancer reassessed the epidemiological, experimental and biological data on exposure to artificial UV radiation from sunbeds. Based in particular on new biological data showing the ability of UVA radiation to induce mutations of the same type as those previously considered specific to UVB or C radiation, the IARC classified exposure to UV radiation emitted by tanning devices as carcinogenic to humans (El Ghissassi, *et al.*, 2009; IARC, 2012).

The data published since then on the carcinogenic effects of UVAs and UVBs support this finding: their effects are very well known and documented. The carcinogenic effect of UV exposure from tanning devices for cosmetic purposes, particularly when exposure began at a young age, has been described in numerous reports and/or opinions of health agencies in France, as well as at European and international level. The UV doses received during artificial-tanning sessions add to the doses received in daily life, at work and/or during leisure activities and holidays, and given the stochastic nature (i.e. by a probabilistic effect) of the skin cancer induction mechanisms, it is not possible to define a safety dose for UV exposure to tanning devices (SCHEER, 2016).

In its Opinion of 3 July 2014, ANSES stressed that the regulatory mechanism resulting from Decree No. 2013-1261 of 27 December 2013 constituted a partial and insufficient response in light of the proven risk of skin cancer for tanning booth users. It recommended that all commercial use and the sale of devices be eventually stopped. The Agency noted that Article 21 of Act No. 2016-41 of 16 January 2016 (known as the Act on the modernisation of the health system) formulated new restrictions (ban of the marketing of equipment not intended for professional use, various bans on promotion) designed to strengthen regulation of the activity (both regarding the devices and the training of professionals).

Nevertheless, the examination of the new data carried out in the context of this formal request has consolidated the previous scientific knowledge and assessments. ANSES therefore stresses the carcinogenic effect for the population of exposure to artificial UV radiation and recommends that the public authorities take the necessary steps to prevent the general population from being exposed to artificial UVs for cosmetic purposes.

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KEYWORDS

Rayonnement ultraviolet, UVA, appareils de bronzage, cabine de bronzage, cancer, mélanome

Ultraviolet radiation, UVA, sunbed, cancer, melanoma

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ANNEX 1

Presentation of participants

PREAMBLE: The expert members of the Expert Committees and Working Groups or designated rapporteurs are all appointed in a personal capacity, *intuitu personae*, and do not represent their parent organisation.

RAPPORTEURS

Jean-François DORÉ – Emeritus Research Director at the National Institute of Health and Medical Research (INSERM)

Thierry DOUKI – Head of Laboratory / Doctor Engineer in Chemistry, French Alternative Energies and Atomic Energy Commission (CEA)

EXPERT COMMITTEE

Anne PEREIRA DE VASCONCELOS – Research Manager, French National Institute for Health and Medical Research (INSERM), Laboratory of Cognitive and Adaptive Neurosciences – UMR 7364, CNRS – University of Strasbourg

Members

Thomas CLAUDEPIERRE – Lecturer and researcher at the University of Lorraine

Brigitte DEBUIRE – Emeritus University Professor

Jean-François DORÉ – Emeritus Research Director at the National Institute of Health and Medical Research (INSERM)

Thierry DOUKI – Head of Laboratory / Doctor Engineer in Chemistry, French Alternative Energies and Atomic Energy Commission (CEA)

Jack FALCON – Emeritus Researcher at the Museum of Natural History, National Centre for Scientific Research (CNRS)

Emmanuel FLAHAUT – Research Director at the National Centre for Scientific Research (CNRS)

François GAUDAIRE – Engineer at the French Scientific and Technical Centre for Building (CSTB)

Martine HOURS – Doctor and Epidemiologist, Research Director at the French Institute of Science and Technology for Transport, Development and Networks (Ifsttar)

Chaker LARABI – Lecturer and researcher at the University of Poitiers

Joël LELONG – Assistant Laboratory Director / Doctor of Physics, French Institute of Science and Technology for Transport, Development and Networks (Ifsttar)

Frédérique MOATI – Lecturer in Biophysics and Nuclear Medicine, University Paris Sud XI / Hospital Practitioner / Radiopharmacist / Biologist, AP-HP Bicêtre Hospital

Catherine MOUNEYRAC – Director of the Institute of Biology and Applied Ecology and Professor in Aquatic Ecotoxicology at the Catholic University of the West (UCO)

Fabien NDAGIJIMANA – University Professor, Joseph Fourier University, Grenoble

Anne-Lise PARADIS – Research Manager at the National Centre for Scientific Research (CNRS)

Marie-Pierre ROLS – Research Director at the National Centre for Scientific Research (CNRS)

Valérie SIMONNEAUX – Researcher in Neurobiology of Rhythms at the National Centre for Scientific Research (CNRS)

Alain SOYEZ – Laboratories Manager, Consulting Engineer, Nord-Picardie Occupational Health and Pension Insurance Fund

Esko TOPPILA – Professor, Research Director at the Finnish Institute of Occupational Health, Helsinki, Finland

Alicia TORRIGLIA – Doctor, Director of Ophthalmology Research, Cordeliers Research Centre, French National Institute for Health and Medical Research (INSERM)

Françoise VIENOT – Professor at the National Museum of Natural History, Head of the "Vision, Light and Appearance" team at the Centre for Research on Conservation of Collections (CRCC)

Catherine YARDIN – Professor, Head of Department, Doctor and Biologist at the Dupuytren Hospital, Limoges University Hospital

ANSES PARTICIPATION

Scientific coordination

Olivia ROTH-DELGADO – Scientific Project Manager – ANSES

Scientific contribution

Olivier MERCKEL – Head of the Unit for Physical Agents, New Technologies and Development Areas – ANSES

Olivia ROTH-DELGADO – Scientific Project Manager – ANSES

Administrative secretariat

Sophia SADDOKI – ANSES

ANNEX 2

Regulations on the use of tanning devices

In the 1980s and 1990s, Norway, Sweden and France were the first countries to take measures to regulate the use of artificial tanning, such as a ban on minors, a ban on devices with free access, and the requirement to declare installations, train operators and inform users. A number of countries or states subsequently regulated the use of tanning devices. In Europe, by 2014, 14 countries had banned their use by minors, but the regulations are far from being harmonised within the European Union. In Canada, most provinces have prohibited access for minors. In the United States, the situation is complex, with the states regulating the use of artificial tanning; and while almost all states have adopted regulatory measures, only eleven states, including California, have prohibited minors from using them (see the 2016 SCHEER report for a more complete description). The WHO's Intersun programme, in collaboration with the Directorate General for Health, established and placed online in 2017 a database of national regulations (Sunbed legislation database, WHO 2017 – http://www.who.int/gho/phe/ultraviolet_radiation/en/).

In November 2009, following the International Agency for Research on Cancer's classification of UV radiation emitted by tanning devices as a Group 1 carcinogen and based on the impossibility of defining a safe threshold dose, Brazil was the first country to completely ban the sale and use of tanning devices for cosmetic purposes (RDC No. 56, 2009). Since January 2016, all Australian states have had an outright ban on the commercial use of tanning devices. This measure was rapidly implemented through incentives and strong enforcement (Sinclair *et al*., 2016).

In June 2017, the WHO compiled the recommended actions for regulating the use of artificial tanning in a document ("Artificial tanning devices", 2017). This project was supported by the French Ministry of Health and funded by ANSES and the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA). The recommended measures range from restricting access to certain population categories, along with operating conditions and information for users, through to prohibiting the rental or sale of appliances for domestic use, and a total ban on artificial UV tanning devices (see Figure 1).

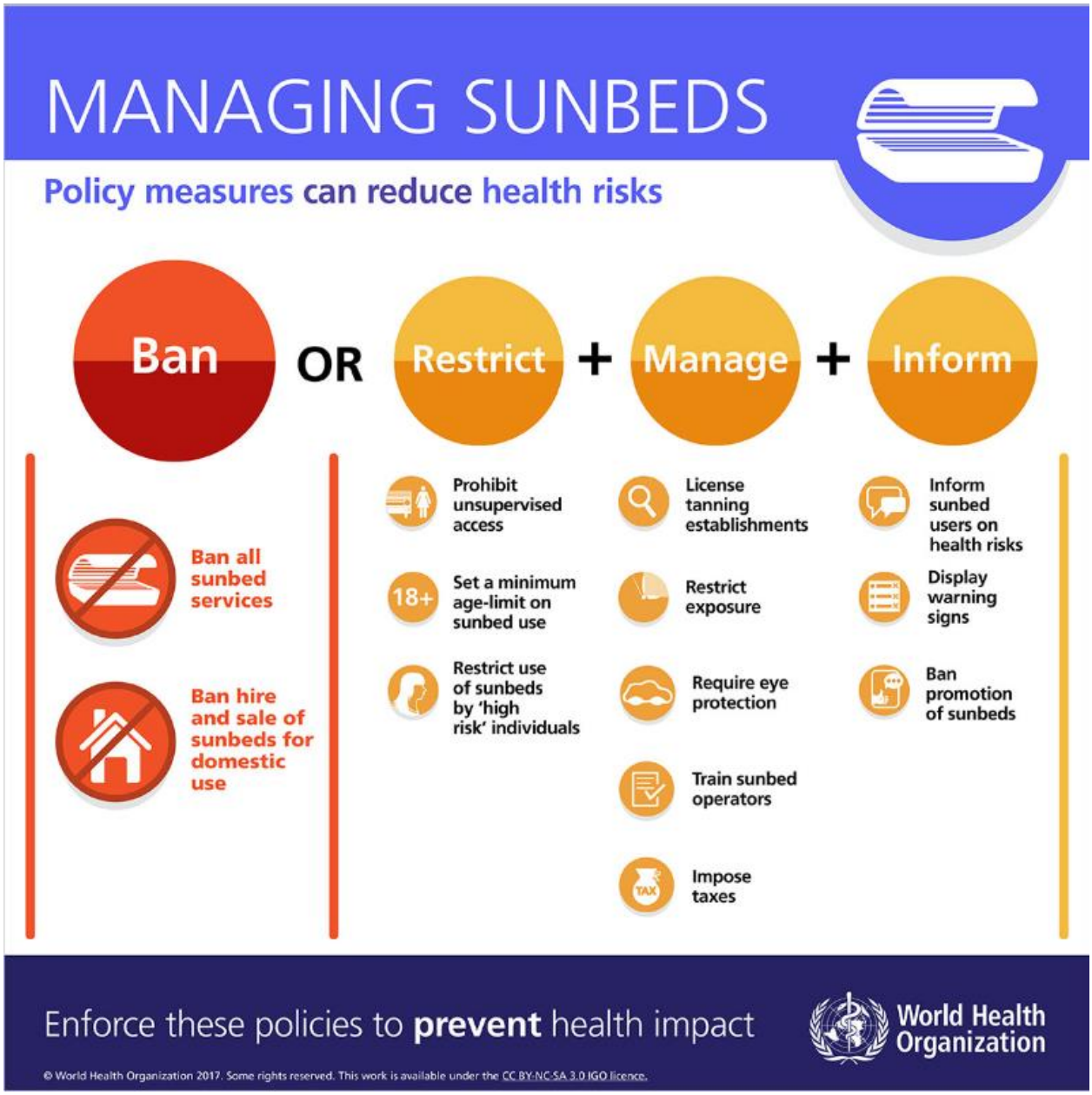

Figure: 1 Regulations to reduce the health risks of UV tanning devices (source: Artificial tanning devices: public health interventions to manage sunbeds, WHO, 2017)