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Institut de Veille Sanitaire

afssaps

ULTRAVIOLET RADIATION

CURRENT KNOWLEDGE OF EXPOSURE AND HEALTH RISKS

May 2005

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Letter received on
2 Sept. 2004
7183

MINISTRY OF ECOLOGY AND SUSTAINABLE DEVELOPMENT
Economic Studies and Environmental Evaluation Department

MINISTRY OF HEALTH AND SOCIAL PROTECTION
Health Directorate-General
Paris, 06 Sept 2004
From:
Director-General of Health
Director of Economic Studies and Environmental Evaluation
to:
Director-General of the French Environmental Health Safety Agency
The Director of the Health Watch Institute

Re: *Constitution by Afsse of a group of experts responsible for evaluating the health risks associated with the use of tanning installations that emit ultraviolet radiation, and examination by InVS of the feasibility of studies enabling the exposure of the French population to UV radiation to be characterized.*

Encs.: Afsse note on the risks associated with UVA dated 19 April 2004
Referral to Afssaps on UVA radiation dated 14 April 2004

The opinion from Conseil Supérieur d'Hygiène Publique de France – CSHPF (the French Higher Public Health Council) dated 4 April 1996 led to the regulation of suntanning practices in tanning establishments and control of their application. Recently, two reports by the National Academy of Medicine dated March 2003 and May 2004, and the Afsse note dated 19 April 2004, drew the attention of the public authorities to the danger of exposure to UVA radiation.
You are therefore requested to reassess the health risks associated with exposure to radiation of natural origin and the use of tanning installations in accordance with the procedures defined in the schedule to this letter. These procedures have two aspects. The first relates to the current state of scientific knowledge, and will form the subject of recommendations to the public authorities. The second will define the work needed to characterize the exposure of the population to ultraviolet radiation.
We hope that the two documents requested can be delivered by the end of the first quarter of 2005.

Copies: Afssaps
DGS/SD3
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Appendix – Description and organization of work

1. State of scientific knowledge

Afsse has been requested to set up a working group which includes (among others) representatives from the Health Watch Institute and the French Health Products Safety Agency. This working group is to prepare an experts' report on the following subjects:

- articles published or in press relating to the health effects, and especially the carcinogenic effects, of exposure to UV radiation and the use of tanning installations which emit ultraviolet radiation. The review of the existing literature will adopt a critical position, taking account of the specific features of the French situation (intermediate skin phototypes, types of UV radiation authorized by French legislation);
- the relevance of using limit values based on the minimal erythema dose (inducing acute effects) to evaluate carcinogenic risks (melanoma, basal-cell and squamous-cell epithelioma);
- the relevance of the use of sunlamps which only emit UVA radiation;
- the justification for prohibiting the use of all cosmetic products during sessions in tanning booths, especially antioxidant substances;
- the most relevant European and international scientific and regulatory positions designed to regulate tanning devices that emit ultraviolet radiation. A comparative study will be envisaged for this purpose.

2. Characterization of exposure

At the same time, in order to characterize the exposure of the French population, a second working group will be set up by the Health Watch Institute. Afsse and Afssaps will be represented on this working group, whose role will be to propose study projects designed to investigate and specify the risks associated with exposure to UV radiation (the proportion of the population exposed to UV radiation, exposure practices, existence and frequency of accidents, extent of photodermatitis, immunodepression, etc.). The feasibility of these studies will be examined by the working group, which will issue concrete proposals designed to allow evaluation and surveillance of the population's exposure to UV radiation.

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Preamble

History of UV risk management in France

The carcinogenic action of UVB radiation has been known for a long time. It was long believed that UVA radiation presented no danger to health, and could be used as a tanning aid. However, following a referral to the Health Ministry by the Consumer Safety Commission (CSC) in 1995, a working group of the French Higher Public Health Council (CSHPF), requested by the Directorate-General of Health to evaluate the risks of using tanning apparatus, cast doubt on the harmlessness of UVA radiation in 1996. It proposed to CSHPF the basis for legislation designed to limit the use of UVA tanning devices. This legislation was passed in the form of Decree no. 97-617 of 30 May 1997, relating to the sale and availability to the public of certain types of tanning devices using ultraviolet radiation, and its implementing regulations. Similar, and sometimes identical legislation was subsequently passed in several countries, especially in Europe.

Decree no. 97-617 of 30 May 1997 introduced several innovations:

- minimum conformity of equipment used for artificial tanning purposes to the international safety standards governing this type of equipment;
- compulsory notification of operation of tanning installations to Prefectures;
- regular technical inspections of installations by approved organizations;
- personnel training regarding the risks associated with the use of ultraviolet radiation;
- obligation to give information to the public in artificial tanning establishments and at the time of sale of tanning devices to the public;
- prohibition on use of tanning installations by minors;
- limitation of use to only the UV1 and UV3 equipment defined in French standard NF EN 60335-2-27, which are the types with the lowest irradiation levels.

These regulations, designed to give the using public a guarantee of the safety of the installations made available to them and comprehensive information about the risks involved, were brought into effect gradually. Technical inspections of tanning installations were introduced in 1999. To date, some 8000 establishments have been inspected by 9 organizations approved by the Ministry of Health to inspect this equipment. Some establishments which do not specialize in tanning (especially in the hotel industry and sports establishments) are not usually notified. Personnel training has been organized since the end of 1997. At the beginning of 2005 there were some 500 trainers responsible for giving training in beauticians' schools, vocational colleges and the various vocational training centres offering training for beauticians, with an estimated total of 12,000 installations. However, there is a high rate of opening and closing of these installations in France, and a high turnover of training personnel.

Context and aims of the referral

Although the risks associated with exposure to UVB radiation have long been known, the mutagenic activity of UVA radiation has been known for less than 10 years. In 1995, the Canadian team led by Drobetsky (Drobetsky et al., 1995) demonstrated for the first time in Chinese hamster cell cultures that UVA radiation induces genetic "signature" mutations different from the UVB signature mutations which were already known and identified in human skin cancers. The following year, a French team comprising CNRS (National Scientific Research Centre) researchers and clinical practitioners from St Louis Hospital, led by Alain Sarasin (Robert et al., 1996), demonstrated that UVA radiation can be as mutagenic as UVB radiation for human cells.

Nevertheless, some epidemiological studies failed to demonstrate the existence of a major risk. However, in 2002, an American study showed that the risk that users of artificial tanning devices will develop squamous-cell skin cancer is multiplied by 1.5, and the risk of developing basal-cell skin cancer is multiplied by 2.5. More recently, in November 2003, a large cohort study conducted on over 100,000 Norwegian and Swedish women, monitored for 8 years, showed that the risk of melanoma associated with the use of tanning devices at least once a month is multiplied by 1.5 (2.6 for people aged 20-29) (Veierød et al., 2003).

The National Toxicology Program in the USA classified UVA radiation as probably carcinogenic in man in its 10th Report on Carcinogens published in November 2002.

Finally, in 2004, the team led by Gary Halliday of the Sydney Melanoma and Skin Research Institute published results in the Proccedings of the US National Academy of Science (Agar et al., 2004) demonstrating that UVA radiation can play a central role in the malignant transformation of human epidermis stem cells. This team studied the specific lesions and mutations associated with UVA and UVB radiation. It demonstrated that UVA mutations are found in the germinative basal layer of the epidermis, while UVB mutations are situated higher in the epidermis; this corresponds to penetration of different ultraviolet wavelengths into the epidermis, UVA penetrating more deeply than UVB.

All these results demonstrate that ultraviolet radiation with a high wavelength have major implications for public heath as regards the risk of skin cancer. These aspects will be discussed in greater detail later in this report.

The attention of the public authorities was drawn to the risk of exposure of the population to ultraviolet radiation in two reports issued by the National Academy of Medicine in March 2003 and March 2004, and in the note issued on 19 April 2004 by Afsse which, in the context of its science watch mission, wished to report on the current state of knowledge concerning the risks associated with natural and artificial ultraviolet radiation and inappropriate use of sun protection products. The health and environment ministries asked Afsse to reassess the health risks associated with exposure to ultraviolet radiation of natural origin and the use of tanning devices. Afsse set up a group of experts including representatives of the Academy of Medicine, IARC, members of Institut National de la Santé et de la Recherche Médicale – Inserm (National Institute of Health and Medical Research) research laboratories and dermatologists specialising in this field, as well as InVS and Afssaps to which the referral was directed, to answer the questions posed in the Ministry's referral:

- to review articles published or in press relating to the health effects, and especially the carcinogenic effects, of exposure to UV radiation and the use of tanning installations that emit ultraviolet radiation. The review of the existing literature having to adopt a critical position, taking into account of the specific features of the French situation (intermediate skin phototypes, types of UV radiation authorized by French legislation);
- to evaluate the relevance of using limit values based on the minimal erythema dose (inducing acute effects) to evaluate carcinogenic risks (melanoma, basal-cell and squamous-cell epithelioma);
- to evaluate the relevance of using sunlamps which only emit UVA radiation;
- to justify a prohibition on the use of all cosmetic products during sessions in tanning booths, especially antioxidant substances;
- to present the most relevant European and international scientific and regulatory positions designed to regulate tanning devices that emit ultraviolet radiation in a comparative study.

However, as the consequences of exposure to natural and artificial ultraviolet radiation are hard to differentiate in terms of global effects, the group of experts decided to base their report on a global analysis of UV risk. In addition to the objectives stated in the referral, Afsse extended the study to the possible risks associated with domestic use (in the home or public places such as offices and schools) of lamps known as "full-spectrum" lamps which emit ultraviolet radiation above the visible spectrum, including large proportion of UVB radiation according to the available documentation. This marketing of lamps destined for the general public is recent, and performed through distribution circuits in specialist shops or over the Internet. This distribution is still very marginal, but could develop more widely. The experts' group also considered the possible consequences of using sun protection products, whose efficacy basically focuses on UVB radiation, as the use of these products can lead to an increased duration of exposure, and therefore an increased risk associated with exposure to UVA radiation.

InVS and Afssaps have been asked to report on different aspects of ultraviolet radiation. In parallel with the referral to Afsse, a second working group has been set up by InVS to characterize the exposure of the French population (proportion of the population exposed to UV radiation, exposure practices, existence and frequency of accidents, etc.). Afssaps has prepared a report on "ultraviolet radiation and use of cosmetic products". The work of the various working groups is presented in a joint report.

The report should enable the reader to read each chapter resulting from the work of the various working groups separately. There will consequently be some repetition, especially in the definitions.

Introduction

The practice of deliberately exposing the body to sunshine for tanning purposes is a very recent one. For centuries, white skin was the fashion, especially among the upper classes, who believed that dark skin should be reserved for the lower classes. The trend began to reverse in the late 19th century, when health advocates recommended sunbathing for anaemia sufferers. The benefits of sunshine for the synthesis of vitamin D became known in the beginning of the 20th century. Tanned skin rapidly became fashionable with the appearance of paid holidays in 1936, which enabled large numbers of people to go to the seaside in summer. But it was during the 30-year boom period after the Second World War, when the duration of paid holidays increased from one to three weeks, that travel to sunny areas multiplied (winter holidays in the mountains and summer holidays by the sea). Later, in the Seventies and Eighties, the reduction in airline charges allowed many people to fly to tropical destinations. This is when the development of tanning centres began. In just a few decades, a suntan thus became an aesthetic advantage synonymous with good health and high social class.

In scientific terms, ultraviolet radiation is part of the non-ionising electromagnetic radiation spectrum emitted by the sun, in the same way as visible radiation (light) and infrared radiation. Although ultraviolet radiation are invisible to the naked eye, the body reacts to them with protective mechanisms: darkening and thickening of the outer layer of the skin. As a result of their penetration into the skin and their mutagenic potential, exposure to ultraviolet radiation, whether natural or artificial, involves some major medium- and long-term health risks, especially for sensitive populations like children.

The attention of the public authorities was drawn to the risks associated with exposure of the population to artificial ultraviolet radiation in 1997 (Decree no. 97-617 of 30 May 1997 relating to the sale and availability to the public of certain types of tanning devices using ultraviolet radiation, and its implementing regulations). In a referral dated 6 September 2004, the French health and environment ministries asked Afsse and InVS to reassess the health risks associated with exposure to ultraviolet radiation of natural origin and the use of tanning installations. In addition to a review of the current state of scientific knowledge, accompanied by recommendations to the public authorities, the report defines the work needed to characterize the exposure of the population to ultraviolet radiation (referral to InVS).

Understanding the risks of ultraviolet radiation requires firstly a brief introduction to the physics of the various types of radiation, including measurement of ultraviolet radiation, the UV index, the erythema dose and limit values. Secondly, the report will describe the biological and health effects of ultraviolet radiation and analyze earlier experts' reports on the subject. A third part of the report will aim to characterize the behaviour of the French population and its exposure to ultraviolet radiation. Next, the report will assess the usefulness of sun products (referral to Afssaps) and the risks associated with the use of cosmetic products other than sunscreens during exposure to ultraviolet radiation Fifthly, the European and international positions relating to UV-emitting equipment will be described. Finally, the group of experts will issue a number of recommendations to the public authorities relating to exposure to sun, tanning installations and other sources of UV radiation designed for domestic or industrial use.

I The physics of ultraviolet radiation

The main source of exposure to ultraviolet radiation for most people is the sun, However, some individuals are exposed to substantial amounts of UV radiation originating from artificial sources, including apparatus used for tanning purposes, industrial sources (such as welding arcs, paint polymerisation and reproduction work), domestic sources (halogen lighting, "daylight" lighting) and therapeutic medical sources.

I.1 Ultraviolet radiation

Ultraviolet radiation is emitted by natural and artificial sources. It is a portion of the non-ionising part of the electromagnetic spectrum, situated in the wavelength interval between 100 and 400 nm. 100 nm has been conventionally chosen as the limit between non-ionising radiation and ionising radiation with lower wavelengths. Ultraviolet radiation is usually divided into three regions, the limits of which have been arbitrarily determined: UVA (315-400 nm), UVB (280-315 nm) and UVC (100-280 nm). These limits were recently confirmed by the International Commission on Illumination (CIE). However, in the medical sphere and in the field of biology in general, 320 nm is used as the wavelength separating UVA and UVB radiation. It was recently proposed that a distinction should be made between UVA-1 (400-340 nm) and UVA-2 (340-320 nm) radiation.

I.1.1 Solar radiation

The sun is the main source of UV exposure for most people. The broad spectrum and intensity of the UV radiation emitted by the sun result from its very high surface temperature. The levels of UV radiation that reach the earth's surface depend on the time of year, the transmission properties of the atmosphere, and the emission power of the sun. UVA and UVB radiation penetrate the earth's atmosphere, while UVC radiation are absorbed by the stratospheric ozone layer.

Sunlight undergoes absorption and diffraction in the outermost layers of the atmosphere, and then in the stratosphere and troposphere before reaching the earth's surface. Absorption by molecular oxygen (O_2) and absorption by ozone (O_3) are the most important phenomena. The boundary between the troposphere and stratosphere is situated some 10 km from the earth's surface. The stratospheric ozone layer, formed 10-40 km above the earth's surface, in practice prevents all UV radiation with wavelengths under 290 nm (UVC) and a substantial proportion (70-90 per cent) of UVB radiation from reaching the earth's surface. The composition of the solar radiation spectrum at ground level is therefore between 290 and 400 nm.

At ground level, ultraviolet radiation consists of two major components: radiation received directly from the sun and radiation diffracted in the atmosphere. The ratio between direct and diffracted radiation varies with wavelength and the height of the sun above the horizon. Individual exposure to solar ultraviolet radiation depends on geographical location, altitude, time of year, time of day, and possibly cloud cover. Although the reduction in the quantity of stratospheric ozone leads to a forecast increase in terrestrial UV radiation, no significant increase has been documented at our latitudes because of increasing atmospheric pollution and tropospheric ozone. The spectral irradiance of ultraviolet radiation (at 300 nm) is theoretically at its peak at midday (local solar time) when the sun's elevation is at its height. This irradiance is at least ten times

greater than the value observed before 9 a.m. (local solar time) or after 3 p.m. (local solar time). 70 per cent of exposure to ultraviolet radiation is therefore received during the four central hours of the day (local solar time), i.e. from midday to 4 p.m. in summer. Solar irradiance also increases more than 1000 times between 290 and 310 nm.

I.1.2 Artificial UV radiation

Artificial sources of ultraviolet radiation emit a spectrum of radiation with characteristics specific to each source. Its sources are the very different lamps used in medicine, industry, commerce, research and the home. Such sources can produce high amounts of local exposure if used incorrectly.
Conventionally, these lamps can be classified under two types: radiation produced by incandescence and radiation produced by electrical discharge into a gas. The latter will be subdivided according to whether the gas pressure is high or low. The emission bandwidth in discharge lamps depends on the pressure of the gas and the presence of specific additives (metal halides).

"High-pressure" sources

In a sealed source under vacuum, the wall of which consists of quartz to which impurities may be added, an electrical discharge vaporizes mercury, which emits UVA, B and C radiation in a very precise spectrum of radiation. These "high-pressure" sources were used only by the medical profession until 1960. Since then, they have been used for tanning purposes with filtration (ordinary glass suppressing a higher or lower proportion of UVC and UVB radiation, according to the thickness of the glass – UVA radiation pass through it more or less completely, and the UVA-2 fraction, 320-340 nm, may be entirely suppressed).

"Low-pressure" tubes

Since 1960, "low-pressure" tubes have been made according to the same mercury discharge principle, but the silica tube is coated with "powders" which specifically absorb UVC and UVB radiation and release UVA or visible radiation. The composition of the powders can be modified to obtain different types of tubes suited to the user's needs: "narrow-spectrum" UVB tubes, "broad-spectrum" UVB tubes, UVA tubes associated with more or less UVB, and pure UVA tubes. This reflects the different technical characteristics created by the regulatory classification laid down by the international standard CEI 60 335-2-27 – 1985.

Workplace and industrial sources

Except for electric arc welding, industrial sources are generally enclosed, but accidental exposure may still occur. Specific recommendations limiting exposure to optical radiation exist in the form of a voluntary standard (ACGIH 1999). Non-laser optical sources are produced by heating a material to incandescence, by electrical discharge into a gas or vapour, or by excitation of the luminescence of a material.

The emission spectrum of welding arcs depends on the composition of the electrodes and the metals to be welded. The use of this equipment requires major protection of the eyes (full mask with welder's glass which has specific characteristics) and the face, neck and arms in general.

The production of optical radiation by laser is a process similar to that of discharges into a gas. Monochromatic emission may be very high, especially in the ultraviolet and visible spectra. These lasers are mainly used in the semi-conductor industry, which requires extremely high precision. Lasers are also used for cutting processes, and their high intensity makes even very short exposure periods dangerous to the eyes and skin.

Examples of industrial and commercial applications of lamps emitting UV radiation (Table I-1).

Table I-1: Industrial and commercial applications of lamps emitting ultraviolet, infrared and visible radiation

Industrial sphere	Application	Lamps	Emission spectra
Printing	Ink polymerisation	High-pressure mercury Metal halides	UVA UVB, UVC UVA
	Ink drying	Incandescence	Infrared
	Engraving	High-pressure xenon Metal halides High-pressure mercury Fluorescent Tungsten halogen	UVA, visible UVA UVA UVA, visible Visible
Document copying – diazo systems	Exposure	Fluorescent High-pressure mercury Metal halides	UVA, blue UVA UVA
Document copying – zinc oxide	Exposure Fixing	Fluorescent Tungsten halogen Tungsten halogen	Blue, green Visible Infrared
Painting	polymerisation Drying	High-pressure mercury Incandescent Tungsten halogen	UVA, VB, UVC Infrared Infrared
Semi-conductors	Exposure	High-pressure mercury	UVA
Printed circuits	Exposure 	High-pressure mercury Fluorescent	UVA UVA
Chemical reactions	Photochemical reactors	High-pressure mercury	UVA UVA, visible
General reactions	Drying, polymerisation, shrinkage, etc.	Incandescent Tungsten halogen	Infrared Infrared
Cosmetics	Tanning	Fluorescent	UVA UVA
Food hygiene	Insect traps	Fluorescent	UVA
Medical treatments	Skin diseases Psoriasis Vitiligo	Fluorescent High-pressure mercury Metal halides	UVA, UVB UVA, UVB UVA, UVB
	Torn muscles	Incandescent Tungsten halogen	Infrared Infrared
	Hyperbilirubinaemia (neonatal jaundice)	Fluorescent Metal halides	Blue
Germicides Sterilization	Water, foodstuffs, operating blocks, instruments	Low-pressure mercury High-pressure mercury Metal halides	UVC UVC UVB, UVC

Some industrial operations, such as arc welding, also generate the emission of ultraviolet radiation. Office and household lamps using halogen bulbs without a UV filter are liable to generate considerable quantities of UV radiation.

Lamps emitting "natural" light

Low-consumption lamps and fluorescent tubes destined to replace ordinary lamps and lighting tubes are currently available on the market. According to their distributors, these lamps and tubes emit "natural" light which is supposed to imitate sunlight, i.e. with a large UVA and UVB component, the proportion of UVB apparently being greater than in suntan cabins according to the advertising. Lamps designed for use in industrial processes (drying and polymerisation) have also appeared even more recently on the market destined for the general public, and have been diverted from their original use for use in the home. These lamps emit UV (A, B and C), visible and infrared radiation in varying proportions.

These lamps and tubes are not currently classed as tanning devices, and are sold without any controls in shops or by mail order. However, they manifestly emit artificial UV radiation not conforming to French legislation on UV tanning devices, and in particular do not conform to the technical regulations laid down in Decree no. 97-617 as regards the type of UV equipment on free sale to the public, UVB irradiance (which exceeds the limit established by the decree), and rules relating to the information to be given to the public.

The risk is that the people who use these lamps will be permanently exposed to UVA and UVB radiation, especially in the workplace, as the promoters recommend them for use in offices, shops and even schools, alleging that they have beneficial effects on the health. The levels of exposure to the UV radiation emitted by these lamps are currently unknown. In the absence of standardization of their use, these exposure levels are liable to become high in the event of prolonged use of several tubes or lamps at a short distance as recommended by the manufacturers.

I.2 Measurement of ultraviolet radiation, metrology, UV index, erythemal dose and limit values

I.2.1 Measurement of ambient ultraviolet solar radiation

Solar ultraviolet radiation has been measured worldwide for years. However, coordinated measurements have only been obtained in the last decade, because the databases used for epidemiological studies are still limited, as is evaluation of individual exposure. Ultraviolet radiation detectors marketed or destined for research were only developed recently. Calibration procedures have been improved. A schematic distinction is made between two types of apparatus: fixed spectroradiometers, which can scan the entire spectrum in a few minutes, and broadband dosimeters, which evaluate solar radiation in a few seconds. Individual dosimeters, which are easily installed in a strategic position on individuals, belong to the second type. Broadband apparatus often incorporates a weighting function representative of the biological action spectrum. An erythemal efficacy spectrum is used for epidemiological studies. The uncertainty of measurement of ultraviolet radiation in current practice is relatively large: around 30 per cent.

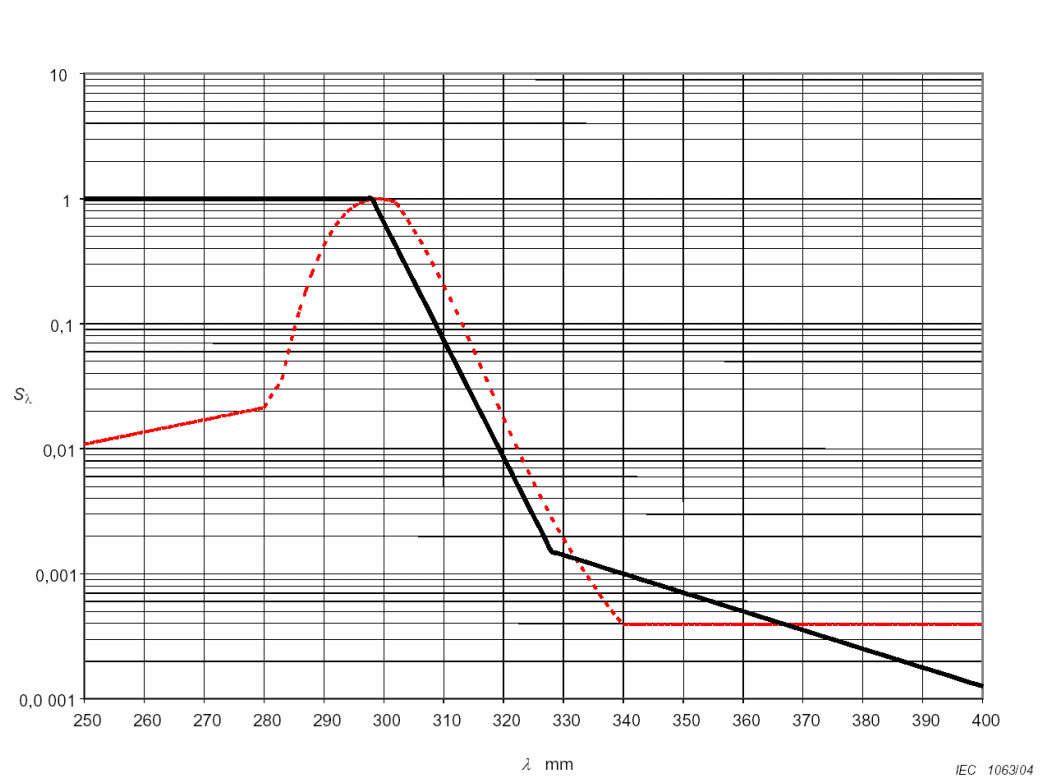
The effective biological UV radiation (UVReff) at a given wavelength is the ultraviolet radiation multiplied by a specific efficacy factor of the biological effect in question (erythema, pigmentation, carcinogenicity, etc.) at that wavelength (see figure of erythemal efficacy spectrum and non-melanoma skin cancer action spectrum, ISO/CIE/CEI standard). Each weighted component is then added to each wavelength in

the range considered. It is expressed in $W.m^{-2}$ (eff) (see weighting factors – Table I-2). These curves are used in standard CEI 60335-2-27 2002 to evaluate the emission limits of tanning devices.

Table I-2 Weighting factor for each wavelength of the non-melanoma skin cancer (NMSC) action spectrum and the erythema action spectrum.

Wavelength (λ) nm	Weighting factor (Sλ)	
	NMSC[a]	Erythema
250	0.010900	1.000000
251	0.011139	1.000000
252	0.011383	1.000000
253	0.011633	1.000000
254	0.011888	1.000000
255	0.012158	1.000000
256	0.012435	1.000000
257	0.012718	1.000000
258	0.013007	1.000000
259	0.013303	1.000000
260	0.013605	1.000000
261	0.013915	1.000000
262	0.014231	1.000000
263	0.014555	1.000000
264	0.014886	1.000000
265	0.015225	1.000000
266	0.015571	1.000000
267	0.015925	1.000000
268	0.016287	1.000000
269	0.016658	1.000000
270	0.017037	1.000000
271	0.017424	1.000000
272	0.017821	1.000000
273	0.018226	1.000000
274	0.018641	1.000000
275	0.019065	1.000000
276	0.019498	1.000000
277	0.019942	1.000000
278	0.020395	1.000000
279	0.020859	1.000000
280	0.021334	1.000000
281	0.025368	1.000000
282	0.030166	1.000000
283	0.035871	1.000000
284	0.057388	1.000000
285	0.088044	1.000000
286	0.129670	1.000000
287	0.183618	1.000000
288	0.250586	1.000000
289	0.330048	1.000000
290	0.420338	1.000000
291	0.514138	1.000000
292	0.609954	1.000000
293	0.703140	1.000000
294	0.788659	1.000000
295	0.861948	1.000000
296	0.919650	1.000000
297	0.958965	1.000000
298	0.988917	1.000000
299	1.000000	0.805378
300	0.991996	0.648634
301	0.967660	0.522396
302	0.929095	0.420727
303	0.798410	0.338844
304	0.677339	0.272898
305	0.567466	0.219786
306	0.470257	0.177011
307	0.385911	0.142561
308	0.313889	0.114815
309	0.253391	0.092469
310	0.203182	0.074473
311	0.162032	0.059979
312	0.128671	0.048306
313	0.101794	0.038905
314	0.079247	0.031333
315	0.061659	0.025235
316	0.047902	0.020324
317	0.037223	0.016368
318	0.028934	0.013183
319	0.022529	0.010617
320	0.017584	0.008551
321	0.013758	0.006887
322	0.010804	0.005546
323	0.008525	0.004467
324	0.006756	0.003597
325	0.005385	0.002897
326	0.004316	0.002333
327	0.003483	0.001879
328	0.002830	0.001514
329	0.002316	0.001462
330	0.001911	0.001413
331	0.001590	0.001365
332	0.001333	0.001318
333	0.001129	0.001274
334	0.000964	0.001230
335	0.000810	0.001189
336	0.000688	0.001148
337	0.000589	0.001109
338	0.000510	0.001072
339	0.000446	0.001035
340	0.000394	0.001000
341	0.000394	0.000966
342	0.000394	0.000933
343	0.000394	0.000902
344	0.000394	0.000871
345	0.000394	0.000841
346	0.000394	0.000813
347	0.000394	0.000785
348	0.000394	0.000759
349	0.000394	0.000733
350	0.000394	0.000708
351	0.000394	0.000684
352	0.000394	0.000661
353	0.000394	0.000638
354	0.000394	0.000617
355	0.000394	0.000596
356	0.000394	0.000575
357	0.000394	0.000556
358	0.000394	0.000537
359	0.000394	0.000519
360	0.000394	0.000501
361	0.000394	0.000484
362	0.000394	0.000468
363	0.000394	0.000452
364	0.000394	0.000437
365	0.000394	0.000422
366	0.000394	0.000407
367	0.000394	0.000394
368	0.000394	0.000380
369	0.000394	0.000367
370	0.000394	0.000355
371	0.000394	0.000343
372	0.000394	0.000331
373	0.000394	0.000320
374	0.000394	0.000309
375	0.000394	0.000299
376	0.000394	0.000288
377	0.000394	0.000279
378	0.000394	0.000269
379	0.000394	0.000260
380	0.000394	0.000251
381	0.000394	0.000243
382	0.000394	0.000234
383	0.000394	0.000226
384	0.000394	0.000219
385	0.000394	0.000211
386	0.000394	0.000204
387	0.000394	0.000197
388	0.000394	0.000191
389	0.000394	0.000184
390	0.000394	0.000178
391	0.000394	0.000172
392	0.000394	0.000166
393	0.000394	0.000160
394	0.000394	0.000155
395	0.000394	0.000150
396	0.000394	0.000145
397	0.000394	0.000140
398	0.000394	0.000135
399	0.000394	0.000130
400	0.000394	0.000126

Figure I-1 Erythema and human skin cancer action spectra



----- Non-melanoma skin cancer action spectrum
—— Erythema action spectrum

The erythema action spectrum is defined by the following parameters:

Table I-3 Erythema action spectrum

Wavelength (λ)	Weighting factor (Sλ)
$\lambda \leq 298$	1
$298 < \lambda \leq 328$	$10^{0.094(298-\lambda)}$
$328 < \lambda \leq 400$	$10^{0.015(140-\lambda)}$

I.2.2 Standard Erythema Dose

The Standard Erythema Dose (SED) measures the erythemal ultraviolet radiation equivalent to effective erythemal exposure of 100 $J.m^{-2}$. The Minimal Erythema Dose (MED) is the dose that produces barely perceptible erythema (with clearly defined edges) in an individual on a defined surface. In general, a weighting function represents the relative efficacy for a particular effect, standardized at the point which is usually most effective. In 1997, the Erythemal Efficacy Spectrum for human skin became an ISO/CIE standard, which allows the erythemal efficacy of a given UV source to be calculated by convolution with the emission spectrum of that source.

I.2.3 UV Index

The UV index is a tool designed for communication to the general public. It is the result of a joint study by the WHO, UNEP, the World Meteorological Organisation (WMO) and the International Commission on Non-Ionising Radiation Protection (ICNIRP). It

has been standardized by ISO/CIE. It expresses the erythemal power of the sun (UV index = 40 x E_{eff} $W.m^{-2}$) (Table I-4), and is usually accompanied by photoprotection advice.

Table I-4 UV Index and Erythema Unit (*) (SED)

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

UV index	Number of erythema units per hour	Strength of sun	Duration of exposure corresponding to the erythema unit (SED)
1	1 SED	Weak	2h20
2	2 SED	Weak	1h10
3	2.5 SED	Average	45 min
4	3.5 SED	Average	35 min
5	4.15 SED	Strong	30 min
6	5 SED	Strong	25 min
7	6 SED	Very strong	20 min
8	7 SED	Very strong	18 min
9	8.5 SED	Extreme	16 min
10	9.5 SED	Extreme	14 min
11	10.5 SED	Extreme	12 min

I.2.4 Limit values

Occupational health medicine (ACGIH) and ICNIRP have established the maximum daily doses that a worker exposed to UV radiation can receive without suffering from acute and long-term effects on the eyes. The cornea is a cellular bilayer highly sensitive to UVB, and above all UVC radiation, which can cause photokeratitis. The maximum daily dose has been fixed at 30 J.m-²Eff, i.e. just under one-third of the SED. This dose takes account of the average cell repair capacity. Table I-5 shows the limits of effective irradiance according to the daily exposure time.

Table I-5 Maximum duration of exposure to UV, based on eye exposure limits (ICNIRP)

Daily exposure time	Effective irradiance: E_{eff} (mW/m^2)
08 hours	1
4 hours	2
2 hours	4
1 hour	8
30 minutes	17
15 minutes	33
10 minutes	50
5 minutes	100
1 minute	500
30 seconds	1000
10 seconds	3000
1 second	30,000
0.5 second	60,000
0.1 second	300,000

There are currently no recommended maximum limits for the human skin, as the “eye” values are low and take no account of the adaptation of the skin as a result of repeated exposure. However, the doses received by the basal layer of the epidermis are of the same order of magnitude as the ocular values. Some 90 per cent of ultraviolet B and 50 per cent and UVA radiation is absorbed by the corneal layer and the Malpighian bodies. To determine the maximum doses for the epidermis, these figures need to be corrected by the coefficient of absorption of the corneal layers and the Malpighian layer on the one hand, and take account of the skin adaptation produced by repeated exposure on the other. Data relating to natural protection and adaptive protection is available for each phototype based on daily infraerythemal exposure for 3 weeks (e.g. holidays) (Table I-6).

Table I-6 Progress of natural photoprotection by adaptation based on exposure to sunlight

Phototype	Day 1-8		Day 8-15		Day 15-21	
	natural protection (*)	adaptive protection	natural protection	adaptive protection	natural protection	adaptive protection
I	1	2	2	3	3	3
II	2	4	4	6	6	8
III	3	6	6	9	9	12
IV	4	8	8	12	12	20
V	6	12	12	16	16	24
VI	10	20 & +	20 & +	20 & +	20 & +	20 & +
0 (vitiligo)	1	1.5	1.5	3	4	4

The values are standardized in relation to the unit (natural photoprotection of phototype I)
(*): the natural protection of phototype I is equal to 2 SED

II The biological and health effects of ultraviolet radiation

II.1 Analysis methodology

In order to be included in this report, scientific papers had to have been published in an international journal after peer review by a Scientific Reading Committee, although not all journals are of equivalent quality. Bibliographical research was performed by consulting the bibliographies of international reports on the subject and the bibliographical databases generally used by scientists. Reports on major studies and published abstracts were also analyzed. Communications made at congresses and symposiums which were not subsequently published were not taken into account.

Each article was examined on the basis of quality criteria corresponding to the field of expertise. For example, in epidemiology, the quality criteria are based on the representativeness of the cases studied, elimination of bias, the quality of information gathering, the choice of exposure indicators and the inclusion of confounding factors, the quality of statistical analysis and the power of the study, depending mainly on the number of cases studied. In biology, these criteria relate to dosimetry, the design of the experiment, statistical processing of the data, and the relevance of the biological models studied.

Each expert was asked to analyze publications appearing in his/her field of expertise; some fields were dealt with by two or three experts, who worked on them jointly.

The conclusions are based on the weight of evidence, including the scientific quality of the studies, their replicability, consistency between studies, and the biological plausibility of the results obtained.

When an expert considered as necessary to consult an external person known for his/her expertise, the inclusion of the information and opinion of that external person was left to the discretion of the expert; this information is not mentioned in specific statements in the report.

II.2 Review of prior experts' reports

II.2.1 IARC Monographs on the Evaluation of Carcinogenic Risks to Humans (IARC, 1992)

The IARC Monographs evaluate the carcinogenic risk of chemical, biological and physical agents, and classify them according to criteria defined in the preamble to each volume, which have remained unchanged since they were established in 1972.

The IARC evaluation of ultraviolet radiation is presented in the table below:

Agent	Degree of evidence of carcinogenicity*		Overall evaluation of carcinogenicity**
	Man	Animal	
Solar radiation	S	S	1
Broad-spectrum UV radiation		S	Not evaluated
UVA radiation		S	2A
UVB radiation		S	2A
UVC radiation		S	2A
Sunlamps and sunbeds use of	L		2A

* L, limited; S, sufficient. ** 1, carcinogenic to humans; 2A, probably carcinogenic to humans.

Epidemiological studies have shown that exposure to sunlamps and sunbeds increases the risk of malignant cutaneous melanoma. The risk increases with exposure time, especially among people exposed before the age of 30 years or those who have suffered sunburn.

II.2.2 Environmental Health Criteria (IPCS, 1994)

This volume in the "Environmental Health Criteria" series, the result of collaboration between the United Nations Environment Programme (UNEP), the World Health Organization (WHO) and the International Commission on Non-ionising Radiation Protection (ICNIRP), is presented as "an authoritative scientific review of environmental and health effects of UV radiation, with reference to global ozone layer depletion ". After summarising the physical characteristics and sources of UV radiation, and some data relating to exposure in humans, the volume presents the current state of knowledge of the health and environmental effects of UV radiation, based on the results of experimental studies conducted *in vivo* and *in vitro* and epidemiological studies. The international recommendations relating to exposure limits, a series of protective measures, and directives relating to current research, are also given. The last part presents evaluations by international institutions.

II.2.3 Risks associated with the use of UV-emitting tanning devices (CSHPF, 1996)

Report written by the "UV-emitting Equipment" Working Group for the "Environmental Health Risks Evaluation" section of the French Higher Public Health Council.

The use of tanning devices which emit ultraviolet radiation has greatly increased since the early Eighties, especially among young people, in France and the rest of the world. In the short term, the main risks associated with artificial UVA radiation are skin burns and photosensitization. In the medium term, exposure to UVA radiation can accelerate skin aging. In the longer term, exposure to artificial UVA radiation appears to be a risk factor for skin cancer. Numerous recent studies have demonstrated the possibility of a direct mutagenic effect of UVA radiation, and some case-control studies have shown that an increased risk of melanoma is associated with exposure to sunlamps and sunbeds. The eyes, as well as the skin, are a target for acute and chronic lesions caused by UV radiation. The interaction between exposure to artificial UVA radiation and exposure to sunlight may also be a source of photoaddition effects.

A French decree classifies equipment under 4 categories and lays down restrictions on their use. Equipment emitting ultraviolet radiation is subject to the regulations applicable to electrical equipment, i.e. the low-voltage decree. The Working Group

recommends a series of measures designed to reduce the risks associated with the use of tanning devices, and strongly discourages its use.

A Recommendation by the Working Group relating to tanning devices that emits ultraviolet radiation is annexed to the report, together with a proposed decree relating to the availability of this equipment to the public, an implementing regulation drafted by the Working Group, and the Swedish, French and European regulations and legislation relating to sunlamps.

II.2.4 IARC Handbooks of Cancer Prevention (IARC, 2001)

The IARC Handbooks evaluate the potential protective effect of agents and compounds against the development of cancer.

Cutaneous melanoma

The results of 15 case-control studies were available to evaluate the potential protective effect of sunscreens against cutaneous melanoma. All these studies are difficult to interpret because of problems of confounding: positive confounding of sunscreen use with sun exposure, sun sensitivity and history of sun-related neoplasia; negative confounding with other sun-protective behaviour (e.g. use of protective clothing, wearing a hat or staying in the shade). Adjustments for these factors seem to be non-existent or insufficient in all studies.

Studies relating to the ability of sunscreens to prevent the development of melanocytic naevi, considered to be precursors of some cutaneous melanomas, suffer from the same problems of confounding as mentioned above.

Basal-cell and squamous-cell carcinoma

The four studies on the ability of sunscreens to protect against basal-cell and squamous-cell carcinoma suffer from the same problems of controlling confounding with individual sensitivity and sun exposure as mentioned above. Two studies have shown that sunscreens have a significant protective effect against actinic keratosis.

Sunscreens can prevent sunburn, and have proven effectiveness in the prevention of UVR-induced provocation of certain cutaneous diseases. Finally, sunscreens may reduce the development of skin aging.

The overall evaluation by the Working Group of the cancer-preventive activity of sunscreens was as follows:

- Topical use of sunscreens reduces the risk of sunburn in humans.
- Sunscreens probably prevent squamous-cell carcinoma of the skin when used mainly during unintentional sun exposure.
- No conclusion can be drawn about the cancer-preventive activity of topical use of suncreens against basal-cell carcinoma and cutaneous melanoma.
- Use of sunscreens can extend the duration of intentional sun exposure, such as sunbathing. Such an extension may increase the risk for cutaneous melanoma.

II.2.5 Artificial tanning sunbeds – risks and guidance (WHO, 2003)

This report summarizes in a few pages the classification of skin types based on sun sensitivity, the biological effects of sunbeds, the reasons why sunbeds represent a public health challenge, recommendations for Government Health Ministries, and recommendations for the management of sunbed operations. These recommendations are the outcome of a workshop held by WHO at the EUROSKIN inaugural conference in 2000.

II.2.6 Exposure to artificial ultraviolet A radiation for tanning purposes (National Academy of Medicine, 2003)

This report clearly and concisely defines the risks associated with sunbed use and the regulatory provisions and legal aspects of the sale and use of sunbeds for tanning purposes:

- Exposure to artificial UV radiation has no health benefits.
- UVA radiations (UVA1 fraction) are as damaging as UVB radiations, and have no immediate symptomatic effects, thus encouraging prolonged exposure, which is even more harmful.
- The increased power of new equipment (same dose in a shorter time) makes exposure to UVA radiation even more aggressive.
- The pigmentation obtained by exposure to UVA radiation does not protect against the harmful effects of solar radiation.
- Artificial UV radiation causes an alteration of epidermal cells, which can lead to the development of skin cancer.
- Individual sensitivity to UV radiation strongly influences the risks of exposure.
- The existence of legislation presupposes that the provision of tanning devices for public use is acceptable in terms of risks.
- The current legislation is widely ignored.

It is necessary to attract the attention of public authorities to the risk of litigation against the government if immediate or delayed harm results from exposure to UV rays.

The National Academy of Medicine:

- advises strongly against the use of sunbeds
- deplores the fact that legislation gives consumers a false impression of safety
- asks public authorities to strengthen warnings and inspections; and
- recommends long-term medical monitoring of anyone who regularly uses indoor tanning appliances.

The National Academy of Medicine has assessed the legal issues raised by the marketing of sunbeds and their availability for public use, stating that this is largely a problem of liability. In practice, any harm caused is the responsibility of the operators (establishments for technical problems, ill-informed personnel, etc.), of the users (knowledge of risks) and of the State.

II.2.7 Sun and Health (National Academy of Medicine, 2004)

This report is an update of a 1997 report on the effects of sunlight on the human body. In view of the biological evidence available since the earlier report, the National Academy of Medicine has formulated a set of proposals and recommendations designed to ensure better prevention in France.

Proposals:

- to campaign against misconception, often based on outdated knowledge
- to give better information about UV irradiation conditions

- to give information about the risks associated with sunburn
- to give better information about protective products and improve their performance
- to promote screening and early diagnosis
- to move towards personalized prevention by identifying the persons at risk.

Primary and secondary prevention:

- use sunscreens and sunglasses which protect equally effectively against UVA and UVB rays
- do not use sunscreens to prolong sun exposure
- give priority to prevention for children (protection of eyes, education)
- improve early screening by developing self-observation techniques
- develop research into the identification of persons at risk (genetic tests, DNA repair tests).

Finally, the report summarizes the biological aspects on which its conclusions are based.

II.2.8 Guidelines on limits of exposure to ultraviolet radiation of wavelengths between 180 nm and 400 nm (incoherent optical radiation) (ICNIRP, 2004)

This report is an update of the report by the International Commission on Non-Ionising Radiation Protection (ICNIRP) entitled "Guidelines on UV Radiation Limits", published in 1996. The IPCS report (IPCS, 1994) was used as scientific basis for establishing new recommendations.

ICNIRP concluded that although the estimated health risks of exposure to ultraviolet radiation are now better understood, recent data do not suggest that the exposure limits proposed in 1989 should be modified. The report thus confirms that the recommendations relating to the limit values established in 1989 are still valid.

The scientific data on which the conclusions and recommendations on the limit values presented in the report are based are summarized in an appendix.

II.2.9 Report on Carcinogens, 11th Edition (National Toxicology Program, 2005)

The 11th and latest edition of the "Report on Carcinogens" by the National Toxicology Program was published in 2005. Solar radiation and exposure to sunlamps and sunbeds were mentionned for the first time in the "Ninth Report on Carcinogens" (2000), and broad-spectrum UV radiation and its UVA, UVB and UVC components in the "Tenth Report on Carcinogens" (2002). Evidence for the carcinogenicity of broad-spectrum UV radiation originates from studies on solar radiation and exposure to sunlamps and sunbeds. The listings for the exposures related to UV radiation are as follows:

- solar radiation is *known to be a human carcinogen*
- exposure to sunbeds and sunlamps is *known to be a human carcinogen*
- broad-spectrum UV radiation is *known to be a human carcinogen*
- UVA radiation is *reasonably anticipated to be a human carcinogen*
- UVB radiation is *reasonably anticipated to be a human carcinogen*
- UVC radiation is *reasonably anticipated to be a human carcinogen*.

Evaluation of exposure to sunlamps and sunbeds is based on sufficient evidence of carcinogenicity from studies in humans, which indicates a causal relationship between exposure to sunlamps and sunbeds and human cancer.

II.2.10 Health Effects from Ultraviolet Radiation (National Radiological Protection Board, 2002)

This important document contains an exhaustive review of the health effects of UV radiation:

- For most individuals, the main source of exposure to UV radiation is the sun. Some individuals may also be exposed to artificial sources, such as sunbeds or medical treatments.
- Some individuals are hypersensitive to UV radiation (photosensitivity) due to genetic or metabolic factors or other abnormalities, or may develop photosensitivity after taking medication.
- The tissues mostly affected are the skin and the eyes. Excessive acute exposure to UV radiation causes sunburn and acute damage to the cornea and connective tissue.
- Chronic exposure of the eyes to UV radiation increases the risk of developing certain connective tissue disorders and cataracts, and may be responsible for macular degeneration of the retina, a major cause of blindness. The relationship with ocular melanoma is uncertain.
- Chronic sun exposure leads to skin aging, and may increase the risk of melanoma and non-melanoma skin cancer. Melanoma is the main cause of mortality from skin cancer. Short, intense exposures such as sunbathing seem to play an important part in the development of melanoma, and possibly of squamous-cell carcinoma. Exposure during childhood is particularly important. Sunbeds represent a major source of intense, intermittent exposure to UV radiation, and consequently represent a potential health risk.
- The main known beneficial effect of exposure to UV radiation is biosynthesis of vitamin D triggered by UVB radiation. However, short periods of everyday life spent outdoors allow a sufficient amount of vitamin D to be synthesized, and additional exposure has no benefits.
- Numerous studies demonstrate that UV radiation has an immunosuppressive effect, but the health significance of this effect is unclear.
- The risks associated with UV radiation can be considerably diminished by reducing exposure (avoiding sunbathing and direct exposure at the hottest time of day, protecting oneself against the sun by seeking shade, wearing suitable clothing and applying sunscreen). Artificial UV sources, especially sunbeds, should also be avoided.

II.2.11 Exposure to Artificial Ultraviolet Light and skin cancer (IARC, under preparation)

A working group of international experts was gathered by IARC to evaluate the risk of skin cancer, especially melanoma, in relation to exposure to artificial ultraviolet radiation for tanning purposes. The working group is currently finalizing a report that will be published by IARC, and a shortened version of the report will be published in a scientific journal.

II.3 Biological effects of UV radiation

II.3.1 Short-term effects

The interactions between UV radiation and the cells are complex phenomena leading to immediate or delayed reactions, which are visible and sometimes painful.

Actinic erythema

This is the classic "sunburn" produced by a sufficient dose of UV radiation. This erythema is induced by disorders caused by absorption of UV radiation by the DNA of the cells and their membrane. These complex lesions cause the release of substances that spread through the epidermis and reach the capillaries, which dilate. Stimulation of the nerve endings causes pain. The intensity and duration of the erythema are proportional to the quantity (dose) of UV radiation received by the various keratinocyte layers.

Classically, the following distinction is made:

- **Traces of erythema:** scarcely visible reddening, not clearly delimited.
- **Erythema 1+:** slight reddening with clearly defined edges, not painful.
- **Erythema 2+:** definite reddening, slightly sensitive.
- **Erythema 3+:** major reddening accompanied by oedema (swelling of papillary dermis), which is very uncomfortable and interferes with sleep
- **Erythema 6+:** this intense, purplish erythema is rapidly accompanied by the appearance of blisters. This is an actual burn, which will leave scars and altered pigmentation.

The Minimal Erythema Dose (MED) is defined as the quantity of ultraviolet radiation, whatever the wavelength responsible, needed to cause slight erythema with clearly defined edges 16-24 hours after exposure. This quantity varies according to the solar sensitivity of the individual. This dose has allowed the construction of the reference erythemal efficacy spectrum (CIE 1987), on the basis of which the erythemal efficacy of all UV-emitting sources is calculated. The effective irradiance of UV equipment must meet the values set out in the table which defines the type of UV sources.

The erythemal efficacy of each wavelength is weighted according to the erythemal efficacy curve, and adjusted to 298 nm (see figure and table). The erythemal efficacy curve can be expressed as mathematical functions as follows:

$EE(\lambda) = 1.0$ $\quad (250 \leq \lambda \leq 298 \text{ nm})$

$EE(\lambda) = 10^{0.094\,(298-\lambda)}$ $\quad (298 \leq \lambda \leq 328 \text{ nm})$

$EE(\lambda) = 10^{0.015\,(140-\lambda)}$ $\quad (328 \leq \lambda \leq 400 \text{ nm})$

In 1997, the CIE recommended the universal use of an erythema unit called the Standard Erythema Dose (SED), the value of which is 10 $mJ.cm^{-2}$ (100 $J.m^{-2}$), standardized according to the erythemal efficacy curve at 298 nm. This unit allows the erythemal power of all UV sources to be calculated.

The speed of appearance of erythema depends on the severity of the sunburn. It will appear a few hours after exposure to UV radiation, culminate within 24-36 hours, and disappear on the 3rd day, to be replaced by evident pigmentation. The erythema may last for over a week. Sunburn may be accompanied by general symptoms (fever, headache and vomiting), depending on the size of the damaged areas and the dose received.

UVB radiation is mainly responsible for erythema, but UVA radiation is also partly responsible.

Actinic erythema should not be observed after exposure to solaria.

Thickening of epidermis

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. This means that after repeated irradiation, provided that there is no blistering, the thickness of the epidermis will have practically doubled, thus shielding the basal layer against the action of UVB radiation. A certain degree of photoprotection is therefore obtained, the extent of which also depends on the neo-melanins synthesized (see below). In the absence of further irradiation, peeling causes the thickened epidermis to return gradually to normal (in 5 weeks).
Long UVA radiation (340-400 nm), which are only slightly absorbed by the epidermis, do not lead to thickening of the skin, and therefore cause hardly any peeling.
Only moderate thickening of the epidermis should be observed after exposure to solaria. This is mainly due to the small amounts of UVB radiation present in the emission of low-pressure UV tubes.

Immediate pigmentation

If sufficient quantities of UVA (10 J/cm²) are received on the surface of the epidermis, the melanins present in the melanocytes and keratinocytes undergo polymerization, which leads to immediate pigmentation that is visible when irradiation ends. This phenomenon is transient. A person who has spent the day in the open air will have a healthy appearance in the evening, but nothing is left the next day. Melano-compromised people do not develop this type of reaction, and their appearance does not benefit from exposure to UVA radiation.
Immediate pigmentation is desired after exposure to solaria.

Adaptive pigmentation (tanning)

Delayed pigmentation or adaptive pigmentation is triggered at higher doses of UVA and UVB radiation. It is visible on the third day after irradiation, and lasts for 3-4 weeks in the case of a single irradiation. This is the tanning reaction.

In the event of repeated exposures, this pigmentation will be increasingly intense, and last longer if peeling remains within normal physiological limits. The melanocytes and melanogenesis are stimulated, both directly by UVA radiation and indirectly by the products of interaction of the UVB radiation absorbed by the keratinocytes. The intensity of tanning depends strongly on the genetic ability to produce melanins (the concepts of phototype and phenomelanogenotype come into play here). In addition to

this neomelanogenesis, which is moderately protective, there is a thickening of the epidermis, which gives melano-competent people a high degree of global photoprotection.

In exposure to solaria, repetition of UVA sessions every 48 hours produces attractive pigmentation in melano-competent people. However, protection against solar radiation remains relatively low, and far from that obtained at the same tanning level caused by a series of exposures to the sun, as there is little thickening of the epidermis.

Production of vitamin D

Exposure to sunlight is perhaps the most important source of vitamin D, because it satisfies the need of most human beings for vitamin D (Holick, 1994). The ultraviolet radiation of the sun triggers the synthesis of vitamin D in the skin (Holick 1994; Holick, 2002). The season, latitude, time of day, cloud cover, fog and sunscreen products modify exposure to UV radiation and synthesis of vitamin D (Holick, 2002). For example, exposure to sunlight from November to February at the latitude of France is insufficient to synthesize enough vitamin D in the skin. Complete cloud cover halves the energy of ultraviolet radiation, and shade reduces it by 60 per cent. Industrial pollution, which increases the screening effect, also reduces solar exposure, and can contribute to the development of rickets in individuals whose dietary intake of vitamin D is insufficient (Wharton et al., 2003). Sunscreens with a protection factor of 8 or more block the UV radiation that produce vitamin D, but it is still important to use sunscreens regularly in order to reduce the consequences of excessive exposure to sun. Initial exposure to solar ultraviolet radiation (10-15 minutes without sunscreen) is sufficient for the synthesis of vitamin D, and should be followed by application of a sunscreen with a factor of at least 15 to protect the skin. 10-15 minutes of exposure of the face, arms, hands or back to the sun at least twice a week without sunscreen is usually sufficient to provide adequate vitamin D synthesis (Holick, 2002). It should be remembered that the vitamin D provided by skin synthesis due to exposure to ultraviolet radiation is merely an addition to the normal dietary intake. Oily fish contains large amounts of vitamin D. For example, a dessertspoonful of cod liver oil represents 3.4 times the daily allowance, and 100 g of mackerel represents 90 per cent of the recommended daily allowance. Finally, a six-year follow-up study of patients suffering from Xeroderma pigmentosum did not show a vitamin D deficiency in those children, despite the total photoprotection used (Sollitto et al., 1997).

During exposure to the sun, irradiation of the skin by UVB radiation causes photolysis of a constituent of the cell membranes, 7-dehydro-cholesterol (provitamin D3), and converts it to previtamin D3, which is found in the epidermis and dermis. Endogenous vitamin D3 reaches the circulation, where it binds to a transport protein. Under the action of excess UVB radiation, the previtamin is converted to inactive lumisterol and tachysterol. This is caused by modulation of vitamin D in the epidermis. The bones accumulate the excess vitamin D produced during spring and summer, which compensates for the production deficiency in winter. This is valuable for pale-skinned people and those living in temperate countries. In people with phototypes V and VI, melanin considerably attenuates UVB radiation, so a real deficiency can be found in northern countries. Whatever the situation, a diet rich in vitamin D can compensate for this deficiency. The hypovitaminosis D observed in some populations does not currently justify exposure to artificial UVB radiation (US NIH, 2004; Australian Health Authorities, 2004).

Two articles recently published on this subject (Hollick and Jenkins, 2003; Gillie, 2004) have been challenged in scientific circles. To defend the beneficial role of artificial UV exposure, the authors review the ability of vitamin D, apart from its role in the prevention of osteomalacia and rickets, to prevent certain cell multiplications and other cardiovascular diseases. These effects were found to be minor, if not negligible in relation to the risk of carcinogenicity involved in UV exposure. The important role played by vitamin D in preventing osteomalacia, infantile rickets and bone fragility (in menopausal women and the elderly) is undeniable. The amount of sunshine in France and the absence of nutritional deficiencies is more than enough to provide a sufficient vitamin D level. Any deficiency can easily be compensated by a few glasses of milk or a balanced diet, especially one containing fish.

The tanning device industry is currently promoting the idea that the vitamin D produced by artificial tanning is necessary. Claims that vitamin D has non-specific antitumoral effects are far from being demonstrated and recognized, and the population does not need a vitamin D supplement provided by UV sessions. The health status of the French population does not justify recourse to vitamin D produced by artificial UV radiation. The WHO has clearly stated that any vitamin D deficiency must be remedied by dietary means, not by exposure to UV radiation (WHO, 2003).

Table II-1 Recommended daily allowance of vitamin D for the French population (Tec. et Doc. Lavoisier, 2000)

Age group	Recommended allowance (µg/day)
Children aged 1-3 years	10
Children aged 4-12 years	5
Adolescents aged 13-19 years	5
Adults	5
Elderly persons	10
Pregnant and lactating women	10

Table II-2 Dietary sources of vitamin D (Tec. et Doc. Lavoisier, 2000)

Foodstuff	Quantity of vitamin D (µg/100 g)
cod liver oil	200
salmon, herrings, anchovies, pilchards	12-20
sardines, rainbow trout, mackerel, margarine	8-12
eel, tuna, oysters, caviar, egg yolk	3-8
river trout, dab, lumpfish roe	1.5-3
mullet, heifer's and lamb's liver, butter, ham, bacon, pâté, mushrooms	0.6-1.5

Keratitis and cataracts

The eyes are naturally protected against intense exposure to solar radiation by the specific geometry of the ocular adnexa: superciliary ridge, eyebrows, eyelashes, eyelids, nasal crest and temporal area. Two reflexes complete this geometrical protection: the narrowing of the palpebral fissure (blinking) and reduction in pupil diameter. This reduces the quantity of ultraviolet radiation accompanying daylight that reaches the sensitive layers of the eye.

Exposure of the cornea to ultraviolet radiation triggers inflammation of the cornea (keratitis) and temporary blindness (snow blindness) in a few hours. These symptoms are reversible in a few days, but in the long term, if repeated, will cause peripheral proliferations (pterygium).

UVA radiations penetrate to the lens, causing opacification of the cells that constitute it in the long term. This central or peripheral opacification constitutes cataracts (progressive loss of vision). It can reasonably be estimated that 400,000 invalidities a year are thus created in France, requiring sometimes major surgery.

There are few risks of acute alteration of the retina. However, observing an intense light source can cause retina burning similar to that observed in people who watch a solar eclipse without protection. This effect is known as "eclipse blindness".

Macular degeneration, a disorder of the retina which leads to progressive blindness that cannot be corrected, is believed to be caused by excessive accumulated quantities of UVA and blue light (see chapter II-3-4).

In view of these serious complications, the potential risks of exposure to artificial UV radiation without eye protection arising from exposure to solaria are evident. Eye protection which filters nearly all UV radiation and part of the visible radiation is essential. Closing the eyes is not enough.

In conclusion

The risks associated with exposure to ultraviolet radiation can be immediately dramatic, or appear later as a result of accumulation of doses. Skin cancer and photo-induced aging are the price of overexposure, i.e. an imbalance between the individual's solar capital and the UV doses received during the lifetime (see chapter III).

Moreover, acute reactions involving both exogenous and endogenous substances are responsible for acute damage which can evolve towards chronicity. Eye protection is essential. The biological effects of ultraviolet radiation of natural (solar) or artificial

origin are similar, and there is no need to use artificial UV radiation to ensure a sufficient supply of vitamin D.

II.3.2 Genotoxic effects

Photogenotoxicity[1]

The alteration in the chemical structure of the DNA may cause the appearance of mutations or lead to cell death. The main types of damage caused by the UVB and UVA components of solar radiation to the DNA are cleavage of the nucleotide chain, covalent protein adducts and products of modification of bases. The nature of the physico-chemical processes at the origin of the modifications caused by exposure to UV radiation depends on the wavelength of the incident photons.

Measurement of DNA lesions by methods such as immunoassays (use of monoclonal or polyclonal antibodies directed against a given type of photodamage) and methods using repair enzymes (such as DNA *N*-glycosylases associated with the comet test) or direct chromatography methods (especially high-performance liquid chromatography associated with tandem mass spectrometry detection (Douki et al., 2000) provides information about the mechanisms and extent of the damage involved in the genotoxic effects of the different types of ultraviolet radiation.

UVB radiation (290-320 nm), the luminous energy of which is directly absorbed by the DNA, mainly induces modifications of the pyrimidine bases (Cadet and Vigny, 1990, Douki et Cadet, 2001):

- **Formation of dimeric photoproducts between two adjacent pyrimidine bases**
  - cyclobutane dimers,
  - pyrimidine (6-4) pyrimidone and Dewar valency isomer photoproducts resulting from strong doses of irradiation or in the presence of UVA.
  - specific UVB irradiation signature: tandem mutations CC $\rightarrow$ TT.

- **Photochemistry of purines in far-UV spectrum**

Although UVB pyrimidine photochemistry is quantitatively the largest, purine photochemistry also presents some interesting features:

- dimerization of adenine, a minor photoproduct whose formation has not yet been observed in cell DNA
- oxidation of guanine to 8-oxo-7,8-dihydroguanine (8-oxoGua) in DNA isolated after exposure to UVB and UVC radiation.

The harmful effects of UVB radiation are largely explained by the formation of dimeric photoproducts of pyrimidines (Douki et al., 2003). The level of formation of 8-oxoGua is 100 times weaker than cyclobutane dimers. The level of these photoproducts in the cell DNA is around one lesion per 10^7 normal bases per $J.m^{-2}$.

UVA radiation and visible light are not absorbed by the DNA. However, the endogenous or exogenous chromophores, in an excited form after absorption of luminous energy, can degrade the genome. This reaction, whose preferential target is the guanine base, is called photosensitization (Pouget et al., 2000) (Ravanat et al., 2000).

[1] Paragraph taken from Afssaps report

Photosensitization reactions to visible light or UVA radiation involve two main mechanisms:

- **The type 1 mechanism** involves an electron or hydrogen atom transfer reaction between the excited photosensitiser and the substrate. The main targets in the DNA are the bases (especially guanine). The latter are converted by an oxidation reaction to an electron in their radical cation. The latter can then react with water or be deprotonized. A secondary reaction of this type I process is formation of the superoxide radical by reaction of molecular oxygen with the anion radical of the photosensitiser; by dismutation, this superoxide radical can generate hydrogen peroxide which, in the presence of a transition metal in reduced form (ferrous ion, for example), is at the origin of the highly reactive hydroxyl radical.

- **The type II mechanism** involves energy absorption by the photosensitiser and transfer on oxygen. This molecule is in an excited state called a "singlet", allowing it to react with the exclusive substrate, the guanine base, specifically to form 8-oxoGua. UVA radiation induces oxidative stress, mainly through type II photosensitization mechanisms. There is also a minority formation of cleavage of DNA chains and products of oxidation of the pyrimidine bases, which results mainly from the action of the hydroxyl radical.

The photo-oxidant aspect of UVA radiation, unless considered as the formation of 8-oxoGua, only seems to play a minor part in the harmful effects of sunlight. The study of 8-oxoGua formation alone is therefore insufficient to define the mechanisms involved in the effect of UVA radiation.

Cutaneous photocarcinogenesis

Skin carcinomas, the most frequent skin cancers in man, are mainly represented by basal-cell carcinoma (BCC), with a slow evolution and local malignity, and the more aggressive epidermoid carcinomas (EC).

The role of exposure to sunlight in the appearance of a carcinoma is established on the basis of clinical, epidemiological and experimental arguments. Cutaneous photocarcinogenesis is attributed 65 per cent to UVB and 35 per cent to UVA, according to a calculation based on the De Gruijld curve (De Laat et al., 1997).
The keratinocytes associated with human EC express more mutations secondary to UVA (formation of 8-oxoGua) than to UVB radiation (cyclobutane dimers) (Agar et al., 2004).

Intermittent and "burning" solar exposure, particularly during childhood, is the main risk factor for melanoma, and has also been established on the basis of clinical, epidemiological and experimental arguments. UVB radiations and, more recently, UVA radiations, are blamed.

The genetic susceptibility and mechanisms involved in photocarcinogenesis of melanoma and carcinoma are very different. The roles played by different wavelengths of the solar spectrum also differ, according to the nature of the cancer. It is therefore reasonable to assume that any protection offered by sun filters against malignant skin tumours must be adapted to the type of cancer to be prevented.

II.3.3 Immunosuppressive effects

The skin's immune defences provide protection against external aggression (bacteria, fungi and viruses). These defences are greatly altered at low doses of UVB and UVA (below the erythema dose). UVB radiation reduces the number of Langerhans cells and reduces their ability to present antigens to the T-lymphocytes. Exposure to UV radiation induces the release of different cytokines (interleukin 10, TNF-α, prostaglandins, etc.) involved in photoimmunosuppression. Moreover, cis-urocanic acid absorbs UVB radiation and isomerizes into trans-urocanic acid which has immunosuppressive properties. This depression is reversible, and its restoration takes around 3 weeks. This phenomenon has only been recognized for a few years, and helps to explain a number of summer disorders (herpes, pityriasis versicolor, impetigo, etc.). Skin tolerance is also involved in long-term tumour promotion. Following exposure to solaria, the skin's defences are lowered, and skin infections have been observed at tanning centres with poor hygiene.

II.3.4 Photo-induced skin aging

Two phenomena are superimposed in skin aging:

- firstly, intrinsic physiological skin aging, a genetically programmed phenomenon associated with morphogenesis and cell maturation, which is accentuated by a deficiency of sex steroids in post-menopausal women and by smoking
- secondly, extrinsic aging, basically created by chronic solar irradiation associated with UVA and UVB radiation, and to a lesser degree with infrared radiation.

Photo-induced skin aging, also known as heliodermatitis, comprises the specific clinical and histological modifications exclusively associated with chronic exposure to the sun, and excludes pre-cancerous and cancerous lesions.

The two types of aging, physiological and photo-induced, are closely linked; however, there are qualitative and quantitative differences between them in clinical, histological, immunohistochemical and biochemical terms. In elderly people, the difference in skin texture between areas usually exposed to the light and protected areas is evident, with a sharp transition on some areas of the body such as the breasts and cleavage, back and buttocks.

Clinical aspects

The clinical manifestations of heliodermatitis are mainly located in uncovered areas: the face (nose and cheeks), back of the hands and forearms. They vary considerably from one person to another, and even between people of the same age and phototype who undergo the same chronic solar exposure (thus indicating individual genetic susceptibility).

Skin lesions may be isolated, but gradually merge, involving:

- thickened, wrinkly, dry skin
- sagging skin which has lost its elasticity
- a yellowish background colour with a sprinkling of telangiectases (indicating attacks on the dermal vascular network) and pigmentary spots (indicating alterations of the melanocytes): hypomelanosis (small colourless marks on the limbs), freckles (small buff-coloured spots) and lentigines (brown spots)

- appearance of small lines, then deeper wrinkles.

Some clinical aspects particularly demonstrate the importance of alterations of the elastic fibres of the dermis (elastosis):

- **citrine skin**, in which the yellowish colour and dimpled surface make the skin resemble lemon bark
- **elastosis of the neck**, which resembles a "plucked chicken skin", consisting of small yellowish-white papules scattered over an erythematous, telangiectatic background
- e**lastoidosis** with cysts and comedones, a combination of yellowish papules, cystic nodules and blackheads on the temples and around the eyes
- **cutis rhomboidalis nuchae**, in which the skin is criss-crossed by deep wrinkles, giving it a "leathery" appearance.

Histological aspects

The histological modifications associated with heliodermatitis concern the epidermis and dermis, but the dermal connective tissue and its cells are the preferential target of solar radiation. The UVA radiation which penetrate deeply into this tissue play a large part in forming these lesions.

The structural modifications of heliodermatitis are very different from those observed in intrinsic skin aging, which is characterized by epidermal atrophy with flattening of all the cell layers and the dermoepidermal junction, and especially by rarefaction of the dermal fibroblasts, whose activity is greatly reduced, which reduces the synthesis of elastic fibres and collagen.

Epidermis

While the stratum corneum is thickened to some extent, the underlying epidermis may be of normal thickness, hyperplastic or atrophic (due to reduction of epidermopoiesis). The keratinocytes may be dysplastic, presenting atypical nuclei and signs of disordered maturation (dyskeratosis, parakeratosis).

The melanocytes are irregularly distributed throughout the basal membrane. Their size and dendricity and the arrangement of the melanosomes are often abnormal, indicating disorders of their melanization functions. Melanocyte density is practically doubled in photoexposed areas, which may explain the appearance of senile lentigines in skin exposed to the sun.

The number and functional activity of the Langerhans cells are reduced in the chronically sun-exposed skin of elderly people. This major loss, amounting to around 50 per cent, may explain the reduction in delayed hypersensitivity reactions and above all the emergence of malignant cell clones at the origin of skin cancers caused by photo-induced immunodepression.

Dermoepidermal junction

The basal membrane is thickened, the dermoepidermal junction is flattened, and the epidermal papillae disappear.

Dermis

In heliodermatitis, the dermis is considerably modified as a result of attack of fibroblasts, elastic and already formed collagens fibres, and of the vascular network.

The pathognomic histological alteration found in heliodermatitis is represented by solar elastosis, which corresponds to dystrophy of the elastic tissue. This elastotic degeneration is situated in the superficial and middle dermis, where thick, fragmented elastic fibres appear in large numbers and become entangled, forming balls of amorphous, granulous material. Under the dermoepidermal junction there is a narrow area (the Grenz zone) which appears to be free of elastosis, but where the fibroblasts are numerous and hyperactive, indicating excessive protein synthesis. The collagen fibres are altered by basophilic degeneration. There is a decrease in the number of mature, insoluble collagen fibres (as a result of degradation under the effect of proteolytic enzymes secreted by the inflammatory dermal infiltrate), while soluble collagen fibres increase. Fundamental substance strongly increases, with elevated levels of proteoglycans and glycosaminoglycans. A moderate inflammatory infiltrate is present in recent lesions, composed of polynuclear neutrophils, lymphocytes and mast cells whose enzymatic secretions are involved in alterations of the macromolecules of the connective tissue. This inflammatory reaction is associated with the action of UV radiation on the dermis. Vascular modifications are numerous, with thickening of the capillary walls, a reduction in the number of capillaries, and focal dilations corresponding to the telangiectases clinically observed. These vascular alterations lead to a major reduction in the oxygen exchange capacity and normal transfer of micronutrients in the dermis.

II.3.5 Photo-induced skin cancers

Some 80,000 new cases of skin cancer are diagnosed in France every year. The number is constantly growing, with an annual increase of 7 per cent. Ultraviolet radiation is the major etiological factor responsible for these cancers, whose aggressiveness depends largely on their histological form. 90-95 per cent of them are the result of proliferation of keratinocytes (basal-cell carcinomas, by far the most frequent, and epidermoid carcinomas, which are rarer), and are highly responsive to simple treatment without a lethal prognosis, while the other 5-10 per cent consist of malignant melanomas (proliferation of melanocytes) with a far more serious prognosis.

For decades, it has been universally recognized that skin cancers are induced by light radiation of solar origin or originating from artificial sources, on the basis of epidemiological and experimental arguments. The mutagenic and carcinogenic effects of UVB radiation in animals and in man have long been known, whereas the oncogenic effects of UVA radiation have only been recognized for a few years. The carcinogenic risk of UV-emitting tanning devices is therefore a topical subject, which can be considered a public health problem.

Photocarcinogenesis is defined as all the phenomena leading to the formation of skin tumours by light radiation. The process of cancerization is the result of damage caused by ultraviolet radiation accumulated in the epidermal cells. Every alteration which escapes the exogenous and endogenous repair mechanisms participates in the various stages leading to cancerization. These processes take one or two decades, proceeding in stages, some of which have clinical symptoms, while others have only manifestations which are histologically detectable (dystrophy, dysplasia) or biologically detectable (gene mutation, appearance of neoantigens).

Skin carcinomas

Basal-cell carcinoma is the most frequent type of skin cancer (60 per cent). It appears after the age of 50, and is mainly located on the skin of uncovered areas: head and neck (90 per cent) and back of the hands. Characterized by a slow, malignant extension, purely local development (no metastasis), it must be destroyed (by surgical excision or radiotherapy), as it becomes insidiously infiltrating and may be a source of local damage.

Epidermoid (or **squamous-cell**) **carcinoma** is less frequent than basal-cell carcinoma (30 per cent of skin cancers). It appears on existing lesions (actinic keratosis, leucoplakia of the lips), and is mainly located in uncovered areas. It is more serious because of its rapid, invasive locoregional development and of its frequency of lymph node extension, although there is a low risk of metastasis.

The carcinogenic role of UV radiation explains the higher frequency of skin cancer:

- in regions exposed to the light (face)
- in people with pale skin (red or blond hair)
- in people who work outdoors (sailors, farmers)
- in people who live in very hot regions (black people are protected by their melanic pigmentation)
- among people who have received heavy doses of artificial UV radiation.

The major carcinogenic effect is due to UVB radiation, namely wavelengths between 290 and 320 nm, with peak efficacy at 293 nm. UVA radiations were long considered harmless, and their carcinogenic efficacy was believed to be negligible. This mistaken idea has been reviewed in the light of recent studies:

- UVA radiations cause fewer tumours than UVB radiations, but only if the irradiation is of short duration (up to 20 weeks). If the irradiation is prolonged up to 250 J/cm^2, just as many tumours are caused by UVA as UVB radiations in most of the models studied, at doses equivalent to those received by intensive UVA tanning enthusiasts (20 minutes' exposure 5 days a week.
- The action spectrum of cutaneous carcinogenesis is parallel to the erythema spectrum up to 313 nm, but if very different beyond, because the erythemal efficacy declines regularly in UVA radiations, while the carcinogenic efficacy, after a decline in the short UVA wavelengths, rises sharply around 360 nm.
- Analysis of erythemal efficacy and carcinogenesis spectra shows that UVB radiation is around 1000 times more effective than UVA in inducing erythema, while the UVA/UVB carcinogenic efficacy ratio is 100. If the spectral efficacy for each of the two effects is related to the relative quantity of UVA and UVB radiation received during natural solar exposure (which contains at least 20 times more UVA than UVB radiation) it will be found that UVB radiation make a 96 per cent contribution to erythema, and around 65 per cent to carcinogenesis, leaving 35 per cent of the responsibility to UVA radiation.

Experimental epidemiological studies confirm that the carcinogenic risk is proportional to the cumulative dose of UV radiation received during the lifetime, but the carcinogenic dose is not known in man. Dose being equal, small repeated doses are more harmful than more intense but less frequent doses.

Cutaneous melanoma

Among the multiple "moles" which some people present, melanoma is fortunately exceptional but extremely serious (over 25 per cent mortality within 5 years), and current treatments have little effect on it. This malignant tumour, consisting of atypical melanocytes, is constantly increasing (its frequency doubles every 12 years), reaching an incidence of 10 new cases per 100,000 inhabitants per annum in Ile-de-France in 1994 (50 cases per 100,00 inhabitants per annum in Australia).

In most cases, melanoma appears in healthy skin in the form of a pigmented spot, resembling a mole but differentiated by its irregular edges (asymmetrical lesion), multicoloured appearance (brown, dark purple, pink or bluish areas) and irregular surface. More rarely (some 25 per cent of cases) melanoma is a degeneration of a mole whose edges, colour and appearance change. As it is extremely serious, melanoma is a public health problem, and it is consequently essential to know whether exposure to UV radiation increases the risk of melanoma.

The number of melanocytic naevi is an essential risk factor

While it is acknowledged that solar exposure constitutes a melanoma risk factor (which accounts for some 65 per cent of melanomas), genetics also play an important part, because they cause several predispositions of the melanocyte system: phototype, genesis of melanocytic naevi, and familial melanomas.

- Some ethnic factors increase the risk of melanoma: pale skin (white people are roughly 100 times more liable to melanoma than black people), tanning difficulty (the decisive factor), liability to sunburn, photoinduced freckles, blond or red hair, grey or blue eyes.
- Early exposure to sun promotes the appearance of melanocytic naevi in children. There is a significant correlation between the presence of a large number of naevi in children and overexposure to sun, whether chronic (over 4 hours a day) or acute (history of sunburn). Although a direct link between naevi and melanomas has not been clearly established, the association between multiple melanocytic naevi and intermittent exposure to the sun is still synergic for melanoma risk.
- A family history of melanoma or dysplastic naevi constitutes a risk factor additional to the risks associated with exposure and phototype.

UV radiation has long been suspect

The role of short wavelength ultraviolet radiation (UVB: 290-320 nm), responsible for sunburn, is suggested by indirect arguments:

- increased incidence of melanoma with decreased latitude (correlated with an increase in UVB radiation)
- high rate of melanoma among people with a deficiency in UVB-induced DNA damage repair processes.

Recently, ultraviolet radiation with longer wavelengths (UVA: 320-400 nm) has also been accused:

- increased incidence of melanoma in Scandinavia compared with southern Europe, which may be explained by different phototypes while UVA irradiance is equivalent, and by "cultural habits": numerous Scandinavians spend a "week

in the Canaries" in winter, leading to sudden, intense exposure because "you need to show you friends that you've been abroad"; for many of them, being able to tan is a sign of good health
- melanoma has been induced in a tropical fish of the Xiphophorus genus by UVA irradiation whose carcinogenic efficacy is only 10 times less than that of UVB radiation in this experimental model
- melanoma risk is doubled by exposure to the artificial UV radiation emitted by sunlamps and sunbeds (see below).

A high level of exposure to sun in childhood is a major risk factor

Exposure to UV radiation undoubtedly plays a part in the genesis of melanoma. However, the elective distribution of melanoma in the areas usually covered by clothes means that a preponderant role is played by intense, intermittent exposure to the sun and clothing habits, with irradiation of the areas uncovered by fashion, like women's legs in the Fifties and Sixties.

Many recent studies emphasize the importance of intense exposure which is responsible for sunburn in childhood or adolescence. Studies of immigrants to Australia, Israel and New Zealand demonstrate that the risk is highest among the white population, and multiplied 3-4 times in the event of migration during childhood. Childhood is therefore a crucial age for the future risk of melanoma. As we have seen, the interaction between phototype, number of melanocyte naevi, solar exposure and history of sunburn is complex, requiring a multifactorial analysis to establish the percentages of responsibility. Equally, exposure to the sun before the age of 15 contributes to the risk of melanoma, and in practice it is advisable to photoprotect adults, and especially children, effectively against UVB and UVA radiation, especially:
- those with a pale phototype who do not tan
- people with multiple melanocytic naevi
- particularly if there is any family history of dysplastic naevi or melanoma.

Action mechanisms

In the genesis of skin cancer, the action mechanisms of UV photons are not fully understood, and in any event are complex and intricate. Photocarcinogenesis is a multi-stage process, in which UV radiation can participate directly or indirectly at all levels: initiation, promotion and transformation. UV irradiation causes numerous epidermal disorders, some of which are strongly suspected of participating in photocarcinogenesis, especially DNA alterations, the production of oxygenated free radicals, and induction of immune deficiency,

DNA alterations

The cell DNA is the main target for aggression by UV radiation. The nucleic acids absorb UVB radiation, which directly creates specific lesions: pyrimidine dimers, addition products and strand breakage. These photoproducts profoundly alter genome expression and are more or less rapidly repaired by complex, almost error-free mechanisms.

UVA radiations alter the DNA directly, and also indirectly through reactive oxygen species, which are responsible for chain breaks, protein-nucleobase bridges and oxidative lesions of bases. These lesions are repaired with frequent errors.

Persistent (unrepaired) DNA damage may be responsible for mutations which profoundly alter the functioning of the genes. The link between this UV-induced damage to the DNA on the one hand and mutation of oncogenes (N*ras*) and tumour-suppressing genes on the other is well established. In particular, gene *p53* regularizes DNA repair by triggering the release of mitosis after repair; it is altered by ultraviolet radiation, and its mutations are strongly involved in tumour promotion.

Free radicals

The generation of oxygenated free radicals during solar exposure to UV radiation has been extensively demonstrated (see Chapter IV-4), and their excessive production is a harmful action which targets proteins, DNA and membrane lipids (lipid peroxidation). This production of free radicals has a number of consequences: membrane ruptures, inactivation of receptors, release of products of peroxidation which are considered mutagenic and cytotoxic, and release of inflammation mediators via arachidonic acid. The role of the free radicals, which are extensively involved in heliodermatitis, seems to be equally important in photocarcinogenesis. Lesion of nucleic acids and DNA repair enzymes can cause malfunctions in cell differentiation and cell behaviour. Moreover, in addition to the attack on the DNA which may occur at the initiation and promotion stage, the free radicals are probably involved in photoinduced immunosuppression and ornithine decarboxylase activity. Production of oxygenated free radicals may be triggered by both UVB and UVA radiation, as studies on cell models clearly demonstrate. It involves the intervention of various endogenous photosensitisers, especially phaeomelanin which, unlike eumelanin, may be involved in these reactions, thus explaining the increased risk of carcinoma in people with blond or red hair.

Immunosuppression

Numerous experimental studies demonstrate that UV radiation (especially UVB, but also UVA) has a suppressant effect on the immune system. This photoimmunosuppression is responsible for a reduction in contact hypersensitivity and delayed hypersensitivity reactions, associated with the presence of antigen-specific suppressor T lymphocytes. UVB radiation may induce local and systemic immunosuppression.

The mechanisms involved in photoimmunosuppression are complex, including:

- a direct action on the epidermal Langerhans cells, whose antigen-presenting function is impaired
- isomerization of trans-urocanic acid into a cis-urocanic derivative with immunosuppressive properties
- production and release of cytokines by the epidermal cells (TNF, IL-1, IL-12 and especially IL-10);
- infiltration of the epidermis by monocytic cells (CD36+, DR+), antigen-presenting cells which may be responsible for the state of tolerance observed after UVB irradiation.

ODC activity

Ultraviolet radiation, via the production of free radicals, increases the activity of ornithine decarboxylase, an enzyme involved in the biosynthesis of polyamines, whose activities increases during malignant transformation.

Carcinogenesis induced by artificial UV radiation

Carcinogenicity of UV radiation

UVA radiation is carcinogenic, and its efficacy, which is admittedly less than that of UVB radiation, has been analyzed in the preceding chapters. This carcinogenic action of UVA radiation is far from negligible, increasing the carcinogenic action of the UVB traces always present in the emission spectrum of the sources used for tanning. Moreover, phaeomelanins present specific absorption in UVA radiation, and may have a carcinogenic effect resulting from photosensitization reactions.

Genotoxicity and mutagenicity of UVA radiation

Although they are not directly absorbed by the DNA, UVA radiation is genotoxic as a result of oxygen-dependent photosensitized reactions. Oxygen activation leads to a cascade of reactions: chain breaks, and bonds between DNA and proteins which are difficult to repair, at least without errors. This type of lesion consequently involves a higher potential risk of mutation than those caused by UVB radiation; in fact, UVA radiation is now considered as mutagenic as UVB radiation.

Initiation and promotion of melanoma

A number of recent experimental studies have found that UVA radiation is involved in the initiation and/or promotion of experimental melanomas; however, extrapolation to man is subject to reservations. An experimental study using the tropical fish Xiphophorus (which has a single anti-oncogene P53) demonstrated that UV radiation can trigger the appearance of melanoma; although UVA radiation are less active than UVB radiation, their carcinogenic efficacy is 100 times greater than their cytotoxic efficacy. In mice with melanoma, the growth and dissemination of the tumour are activated by UVA irradiation.

Epidemiological studies

At least nine case-control epidemiological studies have examined the association between exposure to sunlamps and sunbeds and the risk of melanoma. Six of these studies showed little or no association, but the frequency of use of sunlamps and beds in these studies was very low.

More recently, three more detailed studies, which took account of constitutional factors and natural exposure to sunlight, demonstrated that the risk of melanoma is globally doubled by exposure to artificial UV radiation, and that this risk can be considerably higher in some categories of individuals (see details in paragraph II.3.3).

Ocular melanoma

Some publications have suggested the possibility of a positive correlation between the onset of ocular melanoma and exposure to UV radiation. A recent French publication (Guenel et al., 2001) seems to confirm this correlation.

In conclusion

Skin carcinogenesis induced by ultraviolet radiation constitutes one of the major public health problems, and specific education is required.

The UVA radiation delivered for tanning purposes is considered carcinogenic. In the case of melanoma, this risk appears to be low, but it is doubled in artificial tanning enthusiasts who undergo 10 sessions a year.

The carcinogenic risk of sun and solaria is cumulative. This photo-addition effect is particularly high in inveterate sunbathers who attend weekly UVA sessions all year round; in their case, the risk of developing skin cancer is multiplied by 10.

II.3.6 Dose-effect relationship

There is a dose-effect relationship between the cumulative dose and the risk of non-melanoma skin cancer (see chapter III on exposure behaviour), while there is no simple dose-effect relationship for melanoma (see para. II.3.2).

II.3.7 Medical applications

Dermatologists regularly use phototherapy to treat certain well-defined disorders, especially when other treatments are ineffective or non-existent. The indications and irradiation doses are carefully evaluated, and treatment protocols are applied after being devised by recognized specialists in photodermatology. The various contraindications of phototherapy, which the dermatologist alone can assess, are strictly researched (integument examination, phototype, medicines taken, associated dermatitis, photodermatitis, etc.).

The protocols are adapted to the skin type, and an increase in dose takes account of skin type, the patient's tolerance, and the dermatitis to be treated. The number of sessions is controlled, and the overall dose received is always evaluated and recorded. Monitoring of the patients treated is essential, at regular intervals during the treatment and in the medium and long term after the sessions. Among the recommendations issued during the treatment, it is agreed that a cycle of 20 sessions a year should not be exceeded. The global dose received by patients, whatever the patients and disorders treated, is a tenth of the doses received during tanning sessions.

From the technical standpoint, the equipment is strictly controlled; it operates under the responsibility of a dermatologist, and the radiation emitted is regularly measured.
Exposure to ultraviolet radiation for purely cosmetic purposes is always refused by dermatologists.

The various phototherapies

- PUVA treatment: emission of UVA (broad-spectrum) radiations and prescription of psoralen to be taken orally or applied locally (application or baths) before the sessions
- Phototherapy: broad-spectrum UVB.

More recently:

- Narrow-spectrum UVB phototherapy: 311 nm – TLO1.
- Excimer laser: 308 nm.
- UVA 1 phototherapy (340-400nm).

The disorders treated

Psoriasis was the first type of skin disease to benefit from phototherapy, and the first results immediately showed that phototherapy was exceptionally interesting. Later, T-cell lymphomas were treated, and phototherapy is preferred to more aggressive treatments whenever possible. The most common current applications include PUVA treatment, UVB treatment and UVB 311 treatment, together with the more recent excimer laser and UVA 1 treatments.

Other indications and the wavelengths chosen:
- Vitiligo: UVB 311 or excimer laser
- Lichen planus: PUVA or UVB treatment
- Generalized or localized scleroderma: UVA 1.

Numerous other indications can be envisaged, but the best protocols are often not well established, and there is not a sufficiently large set of studies to confirm their efficacy. The protocols are designed to achieve the greatest efficacy with the lowest doses, but the necessary efficacy/tolerance comparisons are not always well established.

In conclusion

Phototherapy cannot be accepted without very strict medium- and long-term clinical monitoring during treatment. The protocols are designed to achieve the greatest efficacy at the lowest exposure doses, and wavelengths which guarantee the absence of complications are chosen.

Comments

- Dynamic phototherapy is currently being evaluated.
- Extracorporeal photophoreses (*ex vivo* PUVA treatment of blood lymphocytes after leucapheresis) is mainly used to treat lymphoma.
- The treatment of neonatal jaundice is based on exposure to violet light, and is essential to prevent permanent after-effects.

II.3.8 Luminotherapy

The effect of ambient lighting on mood is now well known. It has been demonstrated that bright lighting increases vitality and reduces melancholy in some populations (Einon D., 1997). These observations have led to the use of bright light to treat certain forms of depression (SAD – Seasonal Affective Disorders). The CIE possesses a report (1995) indicating the correlations between different intensities of depression which can be effectively treated by daily exposure to different intensities of light. A specific light receptor, which activates the cells of a ganglion and consequently certain sites responsible for regulating the circadian and neuroendocrine functions, was recently identified in the retina. This pathway is different from the one that induces vision and visual reflexes. Suitable lighting can effectively treat certain disorders, and optimum lighting strategies in relation to health and well-being can be developed. **Ultraviolet radiation is not involved in these mechanisms,** and the necessary quantity of light is around 2500 lux. These quantities are regularly received on clear, sunny days, and are not considered dangerous to the various parts of the eye.

II.4 The health effects of UV radiation

II.4.1 The different skin types. Are there any features specific to the French population?

Skin sensitivity to UV radiation

The phototype of each individual corresponds to that person's tendency to sunburn (actinic erythema) and pigmentation (tan). It is imperfectly related to complexion, hair colour, presence of freckles and body hair colour.

Categories of skin sensitivity to ultraviolet radiation, known as phototypes, have been established. They can be defined as follows:

Table II-3 Characteristics of the different phototypes

Phototype	Hair	Complexion	Freckles	Sunburn	Tan
0	White	Albino	0	Always ++	0
I	Red	Milky	+++	Always ++	0
II	Blond	Pale	++	Always +	Slight tan
III	Light brown	Pale	+	Frequent	Pale tan
IV	Dark brown	Dark	0	Rare	Dark
V	Dark brown	Dark	0	Exceptional	Very dark
VI	Black	Black	0	None	Black

The most commonly used simplified classification is the Fitzpatrick classification (Fitzpatrick TB, 1988):
Type I: always burns, never tans
Type II: always burns, sometimes tans
Type III: often burns, always tans
Type IV: never burns, always tans
Type V: moderately pigmented people (brown-skinned Mediterraneans, Asians and Arabs)
Type VI: black race.

Moreover, the sensitivity of each phototype can be expressed by SED units and the corresponding effective erythemal dose. Melano-compromised, melano-competent and melano-protected individuals correspond to a simplification of the phototype classification resulting from consensus by specialists (Fitzpatrick et al, 1995).
The skin cancer registers show that over 90 per cent of people with skin cancer are melano-compromised. These types of cancer are exceptional among melano-protected people.

Table II-4 Sensitivity of the different phototypes

Phototypes	Characteristics	Sensitivity (SED)	Dose ($J.m^{-2}$)
I Melano-compromised	Burns very easily, with no tanning (freckles: always)	2.5 ± 1	150-350
II Melano-compromised	Burns and tans minimally (freckles: sometimes)	3.0 ± 1	200-400
III Melano-competent	Burns and tans moderately	4.5 ± 2	250-650
IV Melano-competent	Burns minimally and tans well	6.0 ± 2	400-800
V	Never burns, tans profusely	7.5 ± 2.5	500-1000

Melano-protected			
VI Melano-protected	Never burns, black skin	12.0 ± 4	800-1200

Melano-compromised people (red-haired phenotype, mutations in the α-MSH receptor) are capable of melanogenesis which has a negative balance in terms of genotoxicity by ultraviolet radiation, leading to major photocarcinogenesis (some 90 per cent of skin cancers).

Melano-competent people present a positive global balance, as the melanin produced effectively protects them against ultraviolet radiation. People belonging to this group account for some 10 per cent of skin cancers, probably because their natural and acquired photoprotection capacity is exceeded.

(Naturally) melano-protected individuals are characteristic of mixed-race, Asiatic and Negroid populations, who only exceptionally suffer from skin cancer, mainly in areas with little pigmentation (e.g. burn scars from which the melanocytes have disappeared). Their natural photoprotection is very high because of the location of the melanosomes, and consequently the melanins, either "capping" in the keratinocytes (Asian population) or in the stratum corneum (Negroid population), where they constitute a protective shield.

This hypothesis, which has been consistently verified in epidemiological studies relating to Australian, American and European populations, is supported by almost daily observation of the absence of skin cancer in vitiliginous areas without melanin or melanocytes, and the high frequency of malignant melanoma and squamous-cell carcinoma in African and Indian albinos. In the latter, melanocytes are present and produce an excess of phaeomelanins due to lack of several enzymes required for eumelanin synthesis.

How are phototypes distributed among the French population?

The available data are based on sporadic studies of particular sections of the French population.

The phototype classification was empirically designed to provide a tool allowing the individual risk of exposure to the sun to be estimated, and suitable protection principles recommended. In view of the highly diversified genetic heritage, individuals rarely present all the characteristics that define a phototype according to the Césarini classification. In practice, the expert's decision to attribute a given type to a given person is partly subjective.

A specific study was conducted in 1998 on the SU.VI.MAX cohort (the SU.VI.MAX "Antioxidant Mineral and Vitamin Supplements" study is a nutritional epidemiological study conducted in France from 1994 to 2003) to describe the frequencies of the characteristics used to determine phototypes according to the Césarini classification on a large sample of French adults at national level, and to study the links between those characteristics (Guinot et al., Sun Reactive Skin Type in a French General Adult Population). This phototype research was conducted on the basis of data collected from 4,912 volunteers: 2,868 women and 2,044 men. However, this cohort cannot be considered statistically representative of the French population.

Significant links have been shown between each characteristic used to determine phototypes according to the Césarini classification and gender.

23 per cent of women said that they had brown or black hair at the age of 20 (as opposed to 32 per cent of men), 38 per cent said they had a dark complexion (49 per cent of men), 12 per cent women reported that they always burn after exposure to the sun (9 per cent of men), and 35 per cent said that they obtained a dark or very dark tan (50 per cent of men). 3 per cent of women had phototype I or II as opposed to 2 per cent of men, 13 per cent phototype IIIa as opposed to 6 per cent of men, 48 per cent phototype IIIb as opposed to 45 per cent of men, and 37 per cent had a phototype ≥ IV as opposed to 47 per cent of men.

The global distribution of individuals between phototypes is as follows:

Phototype I	0.3%
Phototype II	13%
Phototype III	46.4%
Phototype IV	34.2%
Phototype V	6.1%

To study the possible geographical effects, the French regions were arbitrarily divided into two sets: North versus South of France, and West versus East of France. Significant links were found between each characteristic and geographical location: dark complexions were found more frequently in the East (49 per cent) than the West (35 per cent), and in the South (51 per cent) than the North (36 per cent); light brown hair was more frequent in the West (68 per cent) than the East (61 per cent), and in the North (66 per cent) than the South (61 per cent); freckles were more frequently reported in the West (37 per cent) than the East (17 per cent), and the North (30 per cent) than the South (21 per cent); a dark or very dark tan was more frequently reported in the West (47 per cent) than the East (37 per cent), and no tan or a slight tan was more frequent in the North (31 per cent) than the South (26 per cent); the frequency of phototypes V was similar in the West (7 per cent) and East (6 per cent), and less frequent in the North (5 per cent) than the South (9 per cent).

In a recent case-control study (Bataille et al. 2005, in press), the distribution of phototypes in several European Union countries was found to be as follows (Table II-5):

Table II-5 Distribution of phototypes in various EU countries

COUNTRY	EYES			HAIR			PHOTOTYPE[2]		
	Eye colour	Total	%	Hair colour	Total	%	Phototype	Total	%
Belgium	black			black	3	5.5	IV	15	28.3
	brown	19	35.8	dark brown	19	35.1	III	20	37.7
	green	12	22.6	light brown	18	33.3	II	11	20.7
	hazel	2	3.7	auburn	8	14.8	I	7	13.2
	blue	20	37.7	blond	5	9.2			
				red	1	1.8			
France	black	3	1.7	black	8	4.7	IV	54	31.5
	brown	49	29.1	dark brown	45	26.6	III	53	30.9
	green	22	13	light brown	54	31.9	II	44	25.7
	hazel	45	26.7	auburn	46	27.2	I	20	11.6
	blue	49	29.1	blond	14	8.2			
				red	2	1.1			
Sweden	black			black	3	3.1	IV	8	8.5
	brown	11	11.8	dark brown	21	22.3	III	59	62.7
	green	23	24.7	light brown	23	24.4	II	25	26.5
	hazel			auburn	22	23.4	I	2	2.1
	blue	59	63.4	blond	22	23.4			
				red	3	3.1			
Netherlands	black			black	4	2.3	IV	37	21.8
	brown	51	30.1	dark brown	42	24.8	III	88	52
	green	36	21.3	light brown	29	17.1	II	33	19.5
	hazel	2	1.1	auburn	55	32.5	I	11	6.5
	blue	80	47.3	blond	35	20.7			
				red	4	2.3			
UK	black			black	5	3.1	IV	13	8
	brown	40	24.8	dark brown	44	27.3	III	60	37.2
	green	41	25.4	light brown	46	28.5	II	64	39.7
	hazel	12	7.4	auburn	34	21.1	I	24	14.9
	blue	68	42.2	blond	22	13.6			
				red	10	6.2			

[2] In this study, this variable was declared by the subjects, unlike the eye and hair colour variables, which were recorded by the investigator. There is obviously a bias in this declaration; for example, Swedes perceive themselves as less sensitive to sun than the British (De Vries et al., 2005).

Table II-6 Data in the literature relating to the phototypes of the French population

Character-istics of study	No. of cases Age groups studied	Place of study	Author	Results			
				Skin colour	Hair colour	Phototype data	Other data
Evaluation of children's sun exposure	573 children aged 3-15 years	Montpellier	Vernes et al., 1999	85% of children had a fair complexion, 15% had an intermediate complexion	49% of children had light brown hair, 40% were blond, 1% had red hair, and 10% had brown or black hair		43% of children had hazel or green eyes, 34% had brown or black eyes, and 23% had blue or grey eyes
Sun education campaign	228 children aged 9 years	Marseille, Tours, Paris	Bastuji et al., 1999			According to the Fitzpatrick classification, 41.4% of children were phototype I or II, 35% were phototype III, and 23.6% phototype IV-VI	
Sun exposure and habits	200 adolescents (a) aged 13-14 years and 150 children (b) aged 3 years	Marseille	Grob et al., 1993			25% (e) to 28% (a) were resistant to sun; 10% (c) to 11% (a) were moderately resistant to sun; 36% (e) to 42% (a) were moderately sensitive to sun; 27% (e) to 18% (a) were very sensitive to sun	
Evaluation of understanding of sun risk	241 adolescents aged 13-15 years	Saint Etienne	Michel et al., 2000	22% of adolescents said they had a fair complexion	11% said they had blond or red hair		
Study of prevalence of the main types of dermatitis in young people	3,464 young men aged 18 to 24 years	South-east	Buyscaylet et al., 1998	45% of subjects said they had a fair complexion 53% said they had a dark complexion 2% had "coloured" (yellow or black) skin	30% had blond or red hair 63% of subjects had brown hair	38% of subjects had the phenotype characteristics of skin resistant to sun and equivalent to a phototype IV or V (dark complexion and brown hair). 26% of subjects had the characteristics of a skin sensitive to sun and equivalent to phototype I or II (fair skin and blond or red hair)	

Evaluation of frequency of phototypes in a large sample of French adults	2,868 women (35-60 years), and 2044 men (45-60 years on inclusion in the cohort)	National study	Guinot et al.	38% of women said they had a dark complexion, vs. 49% of the men	23% of women said they had brown or black hair at the age of 20, vs. 32% of the men	0.3% phototype I, 2.2% phototype II, 10.8% phototype IIIa, 46.4% phototype IIIb, 34.2% phototype IV and 6.1% phototype V	35% of women said they achieved a deep or very deep tan vs. 50% of men, and 37% of women had a phototype $\geq$ IV vs. 47% of the men

The data are extracted from recent epidemiological studies conducted in France on populations of different ages and origins, and relate to different evaluations of the elements constituting the phototype. Schematically, it can be estimated on the basis of these rather heterogeneous data that some 30-40 per cent of subjects are phototype I or II and 25 per cent are phototype IV or V.

II.4.2 Epidemiological studies – natural UV radiation

Exposure to solar UV radiation (see also chapter III)

The NRPB Working Group has considered the annual exposure values calculated by Diffey as being representative of the exposure of an Anglo-Saxon population. It estimates that this population receives between 3 and 6 per cent ambient UV radiation in temperate countries. The annual value of the UV radiation received by the French population can therefore be estimated, knowing that there is a factor of 3 between the UV radiation received in northern France and that received in the south of the country (average cumulative annual sunshine data supplied by the National Meteorology Board).

Examples of annual exposure:

Office workers	200 SED (exposure at weekends and holidays) = 3-6% of total ambient UV radiation (temperate countries)
Children under 18 years old	300 - 400 SED
Outdoor workers	400 - 800 SED

Melanins and photocarcinogenesis

Epidemiological analysis of skin cancer (melanoma, basal-cell carcinoma and squamous-cell carcinoma) shows that predominantly phaeomelanic populations form the majority of skin cancer sufferers (IARC, 1992).

In 1988 (Césarini, 1988), it was suggested that phaeomelanins act as a carcinogenic agent under UV irradiation. It can now be stated with near certainty that the photoproducts inducing DNA strand breaks are more numerous with phaeomelanins than eumelanins as the wavelength evolves towards the UVA range (Hill and Hill, 1987).

Studies relating to the precursors of eumelanins have produced similar results, clearly demonstrating the production of lesions in the presence of their precursors (Koch, Chedekel, 1986; Land et al., 1986; Miranda et al., 1987; Routaboul et al., 1995; Kipp et al., 1999). Unlike eumelanin polymers, phaeomelanins and eumelanin precursors are soluble, and therefore able to diffuse at all intracellular levels, including nuclear levels, and in the underlying tissues (collagen, elastic tissue, germ cells, pilar cells, etc.). Phaeomelanins and eumelanin precursors are identifiable in the urine; their quantity increases after full-body UV skin irradiation and during pregnancy (role of α-MSH). It can be concluded that only eumelanin polymer is photoprotective, while its precursors are photosensitizing. Actinic erythemas, whether repeated or isolated and intense, are mutagenic and potentially carcinogenic.

The actual photoprotection provided by the melanins must be evaluated not only in qualitative terms, but also on the basis of the kinetics of neomelanogenesis. This demonstrates the

inequality of different types of epidermis in the face of UV aggression, as shown in the table below.

Table II-7 Skin phototypes defined by questionnaire on tanning ability and the appearance of freckles during childhood

No tan	Freckles +++	Phototype I	Melano-compromised
Slight tan	Freckles+	Phototype II	Melano-compromised
Medium tan	No freckles	Phototype III	Melano-competent
Dark tan	No freckles	Phototype IV	Melano-competent
Naturally dark skin	No	Phototype V	Melano-protected
Naturally black skin	No	Phototype VI	Melano-protected

Consensus classification: Fitzpatrick T.B., Cesarini J.P., Young A., Kollias N. and Pathak M.A.

A simple classification perfectly reflecting the ambiguous relationships between UV radiation and melanocytes is proposed in this recent study (Fitzpatrick TB, Bologna JL, 1995) which combines the different concepts of phototypes and melanogenotypes.

Skin cancer

The various types of skin cancer, i.e. melanoma and non-melanoma skin cancers (basal-cell and squamous-cell cancers, described as epidermoid carcinomas by French authors), are now the most frequent types of cancer, and their frequency is increasing among all fair-skinned populations, reaching epidemic proportions. In Australia, recent population studies indicate that the incidence of basal-cell carcinoma in men is over 2 per cent, the incidence of squamous-cell carcinoma is one per cent, and the incidence of melanoma is over 50 per 100,000 (Diepgen and Mahler, 2002). In Europe, it is estimated that although the population of the European Union (25 member states) will remain constant between 2000 and 2015, a 22 per cent increase in non-melanoma skin cancer in persons aged over 65, and 50 per cent in those aged over 80, is to be expected (Boyle et al., 2003).

Numerous factors are involved in the development of these types of cancer, especially pigmentation characteristics (eye, hair and skin colour) and sensitivity to sun (the Fitzpatrick phototype in the strict sense of the term), but sun exposure is one of the most important. However, there are numerous differences between the various types of skin cancer.

Although non-melanoma skin cancer is more frequent in men than women, melanoma is equally frequent in both sexes (though sometimes slightly more frequent in women). A large proportion of melanomas occur in young patients, whereas the incidence of non-melanoma skin cancer increases with age; these types of cancer are clearly an illness of aging populations. Finally, while chronic exposure to solar radiation is clearly a risk factor for non-melanoma skin cancer (although recent results tend to equate basal-cell cancer with melanoma), the risk factor for melanoma is intermittent exposure.

Non-melanoma skin cancer

The epidemiology of non-melanoma skin cancer is far less well known than that of melanoma. In particular, only a little data has been systematically collected from populations. Few registers in Europe and the rest of the world routinely collect notifications of basal-cell skin cancer, and recording of squamous-cell cancer is often incomplete, as these lesions rarely require hospital treatment, and a large proportion are treated without histological confirmation.

Basal-cell and squamous-cell cancer (often collectively described as non-melanoma skin cancers) are the most frequent types of cancer (Table II-8). They account for over a third of all cancers in the USA (approx. 600,000 cases a year). Basal-cell carcinoma is around 4 times more frequent than squamous-cell carcinoma, and both are 18-20 times more frequent than melanoma. However, the incidence estimated by surveying a population is much higher than that recorded in the registers.

Table II-8 Incidence per 100,000, standardized for age, of non-melanoma skin cancers among Caucasians in Australia, the USA and Europe (studies after 1990), according to Diepgen and Mahler, 2002.

Country	Year	Basal-cell carcinoma		Squamous-cell carcinoma	
		Men	Women	Men	Women
Australia					
Townsville*	1998	2055	1195	1332	755
Nambour*	1996	2074	1579	1035	472
Tasmania**	1993	145	83	64	20
USA					
New Hampshire	1991	159	87	32	8
Rochester	1997	175	124	155	71
Others	1994	407	212	81	26
Europe					
Wales, UK	2000	128	105	25	9
Hull, UK	1994	116	103	29	23
Scotland, UK	1998	50	37	18	8
Finland	1999	49	45	7	4
Netherlands	1991	46	32	11	3

* investigation
** register

Epidemiological studies (descriptive studies, cross-sectional studies, case-control studies and cohort studies) of non-melanoma skin cancer were analyzed in detail in a monograph by the International agency for Research on Cancer) (IARC, 1992). This analysis is summarized below.

The descriptive studies revealed a number of characteristics indicating that the risk of skin cancer is associated with sun exposure: host factors, anatomical distribution, geographical distribution and occupational exposure.

Skin cancer mainly effects fair-skinned populations; its incidence is lower among naturally pigmented populations, but a high frequency of squamous-cell skin cancer has been recorded among albinos in those populations. Non-melanoma skin cancer mainly affects parts of the body chronically exposed to sunlight, such as the head and neck. However, a special feature of the anatomical distribution of basal-cell cancer is that it is almost absent from the back of the hands, and rare on the forearms. This cancer also affects parts of the face which receive relatively little light.

Since the late 1930s, the incidence and mortality of non-melanoma skin cancer has been inversely related to latitude, i.e. proximity to the equator. The results of the second national cancer survey in the USA conducted in 1947-48 showed that the incidence doubles every 3° 48’ (approx. 265 US miles) of latitude, from the north to the equator. This gradient is more marked for anatomical locations on the head, neck and upper limbs, all of which are habitually exposed. Several later studies showed an association with local levels of UV irradiation, and studies of immigrants to Australia showed that migration from a less sunny

country is associated with increased risk. Finally, several studies have shown an association between non-melanoma skin cancer and outdoor employment.

Several cross-sectional studies conducted in Europe, Australia and the USA have analyzed a number of sun exposure parameters (job, leisure exposure, sunburn, actinic lesions) in different populations. These studies show that the risk of squamous-cell skin cancer is multiplied by a factor ranging between 1.7 and over 3, depending on the degree of exposure and the exposure parameter. However, while a correlation between the risk of actinic keratosis (a pre-cancerous lesion, the precursor of squamous-cell skin cancer) and squamous-cell skin cancer and the cumulative dose of sun exposure is known, several studies published since the 1990s, especially a study conducted with fishermen in Chesapeake Bay (Vitasa et al., 1990), have begun to indicate that for basal-cell skin cancer the cumulative dose is less important, and intermittent exposure probably constitutes the risk factor.

A dozen case-control studies and at least three cohort studies in the USA and Australia have confirmed these results, and shown that basal- and squamous-cell skin cancers differ in their relationship to sun exposure. While there is a cumulative relationship between sun exposure and the risk of squamous-cell cancer, there is no correlation between the accumulated dose of sun exposure and the risk of basal-cell cancer. Conversely, the risk 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 involvement of ultraviolet radiation, and especially UVB radiation, in the genesis of non-melanoma skin cancer is indicated by the very frequent development of skin cancer in patients suffering from the rare disease Xeroderma pigmentosum, associated with a deficiency in UV-induced DNA lesion repair (Setlow et al., 1969), and characterized by extreme sensitivity to sunlight (Kraemer et al., 1984).

Finally, in a large majority of cases of squamous-cell skin cancer, there is a “signature” UVB mutation of P53 gene; this mutation is already present in actinic keratosis, and precedes the appearance of cancer (Ziegler et al., 1994). Gene p53 is mutated less often in basal-cell cancer (Moch et al., 2001).

Melanoma

The individual risk of melanoma is influenced by host factors (pigmentation characteristics, reaction of skin to sun) and an environmental factor: sun exposure (for a review see Elwood and Gallagher, 1994, Boyle et al., 1995, Armstrong, 2004, Doré and Boniol, 2004). Studies conducted in the 1980s established a correlation between sun exposure and the risk of melanoma, and sun exposure is now considered to be a leading cause of melanoma (IARC, 1992). However, the correlation between sun exposure and melanoma is not a simple one. The total accumulated dose of solar radiation is not the only factor involved, and the type of sun exposure, according to age, plays an important role. Moreover, although the ultraviolet component of the solar spectrum seems to contribute to inducing melanoma, the ultraviolet wavelength(s) which contribute to the development of melanoma are not yet definitely known.

Epidemiological situation of cutaneous melanoma in France

The Health Watch Institute's weekly epidemiological bulletin no. 2/2004 of 6 January 2004 describes the epidemiological situation of cutaneous melanoma in France, and its impacts in terms of prevention.

In France, epidemiological surveillance of cutaneous melanoma is based on mortality and incidence data. However, incident cases of melanoma are only recorded by a dozen General Cancer Registries, which cover no more than 13 per cent of the French population, and do not constitute a sample statistically representative of the whole country. It is therefore necessary to use methods of estimation based on this data.

In 2000, some 7,231 new cases of cutaneous melanoma appeared in France: 42 per cent in men and 58 per cent in women. The 95 per cent confidence interval is wide: 6,132-8,330 cases, because the estimated number of cases is only based on a limited number of cancer registers. Cutaneous melanoma is believed to have been responsible for 1364 deaths in 2000, 704 of them in men (52 per cent), 47 per cent of whom died before reaching the age of 65.

The geographical distribution of the melanoma mortality data in 1993-1997 shows a clear predominance of deaths in Brittany, Pays-de-Loire, Basse-Normandie and Alsace. The lowest rates are observed in Corsica.

Melanoma is one of the tumours whose incidence is increasing most. In France, between 1978 and 2000, the incidence increased by 5.9 per cent per annum in men, and mortality by 2.9 per cent per annum. In women, the incidence increased in the same period by 4.3 per cent per annum, and mortality by 2.2 per cent per annum. A man born in 1953 is ten times more likely to suffering from cutaneous melanoma than one born in 1913, while the factor is six to one for women. The net risk for a man of dying of cutaneous melanoma is multiplied by 2.7 per cent between these two cohorts, while the risk is multiplied by 2.1 for women.

On the international scene, France presents intermediate rates of incidence of cutaneous melanoma; high rates are found in the countries of northern Europe (in Norway 1993-1997: men 14.3/100,000 and women 16.1/100,000), and low rates in southern Europe (Italy, Sassari: men 3.4/100,000 and women 2.6/100 000). This north-south gradient demonstrates the importance of phototypes in the onset of melanoma.

Sun exposure is a risk factor for melanoma

The factors involved in the rapid increase in the incidence of melanoma are by no means fully understood. However, it is clear that the increase in sun exposure of fair-skinned individuals and the method of exposure are involved. The risk of melanoma is higher in individuals who are fair-skinned, have blond or red hair, are sensitive to sunburn, and who develop freckles, than in those with a darker skin (Berwick, 1998).

The conclusion that solar radiation causes melanoma is based on the positive association between melanoma and residence at low latitudes, arguments drawn from studies of migrants which indicate that the risk of melanoma is associated with exposure to sunlight in the place of residence in early life, the anatomical distribution of melanoma, which favours areas regularly or usually exposed to the sun, and arguments drawn from case-control studies and cohort studies which indicate that melanoma is associated with residence in hot climates, is

correlated with solar skin lesions, and is positively associated with intermittent sun exposure and a history of sunburn (IARC, 1992).

The incidence of melanoma in Caucasians is inversely related to the latitude of residence (Boyle et al., 1995). This incidence is highest in countries like Australia, a sub-tropical country where the population is mainly of Celtic origin (MacLennan et al., 1992), and the warmer regions of the USA. The risk of melanoma is associated with the latitude of residence in Australia and the USA, and Caucasian populations living near the Equator are at higher risk then those living near the poles (Jelfs et al., 1994). The situation is less clear in Europe, where the incidence in Scandinavia and Switzerland is higher than in France or Italy (Parkin et al., 2002). This probably reflects different skin pigmentations and the extent of intermittent recreational sun exposure. Conversely, melanoma is rare in dark-skinned people; in the USA, its incidence among African Americans is only a tenth of that found among Caucasians (Parkin et al., 2002). Moreover, although the incidence increases every year among Caucasians in Europe, the USA, Canada and Australia, this increased incidence is very low among the pigmented populations of African or Asian origin in those countries (Boyle et al., 1995)

The risk of melanoma increases among North Europeans who emigrate to Australia and Israel. In those two countries, increased incidence is associated with duration of residence (Holman and Armstrong, 1984, Steinitz et al., 1989). However, for superficial spreading melanoma, emigration to Australia after the age of 20 is not accompanied by increased risk; the highest risk is associated with emigration before the age of 10. In Israel, it has been suggested that in addition to the possibility of sun exposure associated with residence in Israel, there may be an increase in real exposure, probably due to an increase in leisure activities (Steinitz et al., 1999).

Several case-control studies report that subjects who have undergone short periods of strong exposure to the sun, such as residence or employment in tropical or subtropical regions, have an increased risk of melanoma (Table II-9). For example, men who served with the US forces in the Pacific theatre during World War II present a significant excess of melanoma compared with those who served in the USA or Europe (relative risk = 7.7, 95 per cent CI: 2.8 - 21.3). Moreover, the tumours in men who served in the Pacific theatre were more often associated with an existing mole (Brown et al., 1984). More recently, it was shown in a case-control study in Europe that the risk of melanoma is increased by residence in a hot country (adjusted OR = 2.7, 95 per cent CI: 1.4-5.2), and this risk increases further if the subjects take advantage of their stay to sunbathe (OR = 4.7, 95 per cent CI: 1.4 – 13.5), or if they arrived in the hot country before the age of 10 years (OR = 4.3, 95 per cent CI: 1.7 – 11.1) (Autier et al., 1997).

Numerous case-control studies conducted in Australia, the USA, Canada and Europe have studied the association between incidence of melanoma, intermittent sun exposure (occupational and total) and history of sunburn at different ages (Elwood and Gallagher, 1994). These studies were analyzed in detail in a monograph by the International Cancer Research Centre (IARC, 1992). More recently, Elwood and Jopson (1997) conducted a systematic review of 20 case-control studies which analyzed the incidence of melanoma, sun exposure and sunburn (Table II-8). Globally, there is a significant positive association with intermittent recreational sun exposure such as sunbathing (OR = 1.71), a significantly lower risk for intense occupational exposure (OR = 0,86), and a low, almost insignificant risk for total exposure (OR = 1.18). The risk is significantly increased by sunburn at all ages (OR =

1.91), in adolescence (OR = 1.73) and childhood (OR = 1.95). These results clearly show the specificity of the correlation between the risk of melanoma and intermittent sun exposure (reflected by sunburn), contrasting with the reduction in risk associated with intense occupational exposure.

A history of sunburn indicates unaccustomed, intense sun exposure and skin sensitivity. Three major studies in Canada (Elwood et al., 1985), Australia (Holman et al., 1985) and Europe (Autier et al., 1994) demonstrate that the risk of melanoma is associated with the tendency to sunburn rather than an actual history of sunburn.

In addition to the type of exposure, the age of exposure is an important risk factor for melanoma. Studies of immigrants and case-control studies have demonstrated the role of sun exposure in childhood and adolescence. Analysis of a case-control study conducted in Europe shows that the risk of melanoma associated with a given level of sun exposure at adult age increases with stronger exposure in childhood, but that the increased risk is greater than the mere sum of the risks associated with exposure in childhood and exposure at adult age. Strong sun exposure at adult age does not constitute a significant risk factor for melanoma unless there was substantial exposure during childhood (Autier and Doré, 1998). Moreover, analysis of the anatomical distribution of melanoma in relation to the type of sun exposure shows that intermittent sun exposure has greater potential to induce melanoma in people aged under 50, while in older people, melanoma is most often encountered in parts of the body continuously exposed to sunlight (Elwood and Gallagher, 1998).

The risk of melanoma is associated with an environmental factor: sun exposure. However, although it shows a similar geographical and ethnic distribution, melanoma differs considerably from squamous-cell carcinoma in terms of socio-economic class, distribution based on sex and age, anatomical distribution and type of sun exposure. In the early 1980s, these differences gave rise to the hypothesis of intermittent versus cumulative exposure (Holman et al., 1983).

It is therefore not surprising that there is no clear dose-effect relationship between sun exposure and risk of melanoma. Equally, this correlation may appear different according to the country where the study was conducted: a region with strong solar radiation or a more temperate climate. For example, in Queensland the risk increases with total dose, whereas in Western Australia and Canada, the risk increases and then decreases with increased sun exposure, and eventually increases again as a result of the strongest total exposures (Elwood and Gallagher, 1994). The correlation between the risk of melanoma and the dose of solar radiation received is complex, and probably varies with the intermittence of the dose, the age at which it is received, and the characteristics of the host. Intermittent and constant exposure can be intrinsically different, with contradictory effects, with the result that the risk for a given individual depends on the relative contributions made by accumulated and acute sun exposure.

Table II-9 Risk of melanoma associated with short periods of intense sun exposure

Author	Year	Place	Exposure	Risk (RR or OR)	95% CI	P
Paffenbarger et al.	1978	USA	Outdoor work registered with the University's labour medicine department (retrospective cohort study)	3.9		0.01
Brown et al.	1984	New York	Service with the US forces in the Pacific, compared with the USA and Europe	7.7	2.8 - 21.3	0.0002
Elwood et al.	1986	Nottingham UK	Residence $\geq$ 1 year in a tropical or sub-tropical region	1.8	0.6 - 5.1	
Mackie et al.	1989	Scotland	Residence $\geq$ 5 years in a tropical or sub-tropical region	Men 2.6 Women 1.8	1.3 - 5.4 0.8 - 4.0	
Beitner et al.	1990	Stockholm	Residence > 1 year in the Mediterranean, a tropical or subtropical region in the last 10 years	1.9	1.0 - 3.6	
Autier et al.	1997	Europe	Residence > 1 year in the Mediterranean, a tropical or subtropical region	2.7 before the age of 10 years: 4.3	1.4 - 5.2 1.7 - 11.1	

Table II-10 Risk of melanoma and sun exposure.
Results of 29 case-control studies (Elwood and Jopson, 1997)

Sun exposure	No. of studies	No. of cases	Odds Ratio	95% CI
Intermittent exposure	23	6,934	1.71	1.54 – 1.90
Occupational exposure	20	6,517	0.86	0.77 – 0.96
Total sun exposure	11	3,540	1.18	1.02 – 1.38
Sunburn (all ages)	19	4,771	1.91	1.69 – 2.17
adolescence	7	1,826	1.73	1.44 – 2.07
childhood	9	2,732	1.95	1.66 – 2.31

These data demonstrate the specificity of the positive association with intermittent exposure (reflected by sunburn) and the reduced risk associated with occupational exposure.

Exposure to solar ultraviolet radiation is a risk factor for melanoma

Epidemiological arguments indicating that sun exposure is one of the causes of melanoma are supported by biological arguments indicating that the DNA lesions caused by ultraviolet radiation play a central role in the pathogenesis of melanoma.

Patients suffering from Xeroderma pigmentosum, a rare disease (approx. 800 cases worldwide) associated with a deficiency in the repair of DNA photoproducts induced by UV radiation (Setlow et al., 1969), suffer from extreme sensitivity to ultraviolet radiation, and have a greatly increased risk of developing skin cancer: melanoma, basal-cell and squamous-cell carcinoma (Kraemer et al., 1984). 70 per cent of these patients develop tumours at the

median age of 8 years (57 per cent non-melanoma skin cancer and 22 per cent melanoma), i.e. 50 years younger than the population as a whole. These results show the importance of DNA repair mechanisms in the aetiology of melanoma.

It has been demonstrated that the ability to repair DNA lesions induced by UV radiation is reduced in patients suffering from basal-cell carcinoma, a disease that involves a high risk of melanoma (Wei et al., 1995), and that patients suffering from melanoma manifest increased sensitivity to inducement of chromatid breakage by a UV-mimetic mutagen (Wu et al., 1996). More recently, it has been shown that some patients suffering from melanoma present a deficiency in repair of DNA lesions induced by UV radiation (Landi et al., 2002, Pedeux et al., 2002).

Melanoma can be experimentally induced by UV irradiation in animals like the opossum (*Monodelphis domestica*) and freshwater fish (Ley et al., 1989, Setlow et al., 1989). More recently, melanoma was induced by UVB irradiation of human skin grafted onto immunologically tolerant mice (Attilasoy et al., 1998, Berking et al., 2001).

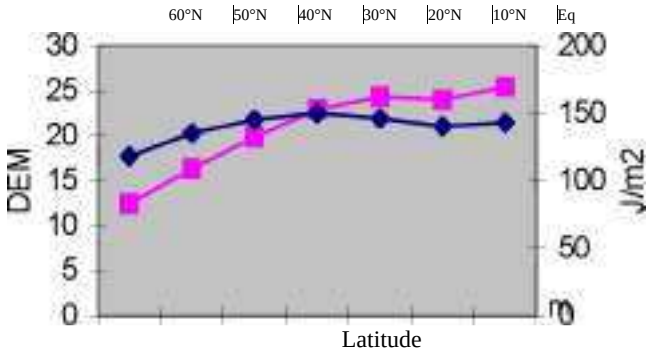
It is believed that the ultraviolet component of the solar radiation spectrum is involved in inducing melanoma (IARC, 1992). In reality, however, the ultraviolet radiation in solar radiation is graduated, increasing from the poles to the equator (Figure II-1). The intensity of UV radiation at a given place varies according to the height of the sun above the horizon, namely the season and time of day, the maximum being observed at the summer solstice, towards the middle of the day, when the sun is at its highest point (zenith). Erythemal intensity (mainly UVB) is nearly three times higher in the one-hour period around solar midday between latitude 60° N and the equator, while the daily erythemal dose only varies by a factor of two due to the fact that the length of the day increases with latitude. For UVA (315-400 nm), the variation with latitude is smaller, because the stratospheric ozone layer absorbs part of the UV radiation and affects erythemal radiation more than UVA radiation. In fact, the ozone layer absorbs all the UVC (100-280 nm) and part of the UVB radiation (280-315 nm), so that the spectrum of UV radiation that reaches the earth's surface is limited to 290-400 nm (Diffey and Elwood, 1994). The intensity of solar ultraviolet radiation also increases with altitude, and as the atmosphere is thinner at high altitude, the solar UV radiation spectrum in the mountains is deviated toward the shortest wavelengths. Moreover, the intensity of solar UV radiation in a given place is influenced by reflection and diffraction (albedo) by snow, water and sand. Thus on a sunny summer's day on a sandy beach, a person under a beach umbrella will be protected against direct radiation, but may be exposed to 80 per cent of the incident UV radiation. Moreover, terrestrial UV radiation is influenced by cloud. Although the influence of cloud on UV radiation is highly complex, its effect on ultraviolet radiation levels can be expressed using a nebulosity factor of 1-0.5C, where C represents the fraction of sky covered by cloud (Diffey et Elwood, 1994). As the size of the water droplets constituting the clouds (2-60 µm) is considerably larger than ultraviolet radiation wavelengths, the transmission of ultraviolet radiation through the clouds is independent of wavelength, and sunburn is possible even when the sun is masked by mist. This can happen in summer in San Francisco, for example.

As the distance between sun and earth is shorter during the austral summer than in summer in the northern hemisphere, and due to the variations in thickness of the ozone layer, the highest levels of ambient erythemal radiation and UVA radiation are observed between 20 and 30° latitude south in December and January. It is therefore not surprising that the maximum incidence of melanoma is observed in the southern hemisphere, and that epidemiological

studies conducted in areas of strong ultraviolet radiation like Queensland tend to indicate that melanoma risk is affected by the total accumulated sun exposure, thus reflecting the high level of exposure to ultraviolet radiation throughout the year. Conversely, in studies conducted in temperate climates like Canada and Europe, strong ultraviolet radiation is recorded during the holidays, and is reflected by intermittent exposure of sunbathers.

There is currently a fairly broad consensus that melanoma is caused by exposure to solar ultraviolet radiation. Armstrong and Kricker (1993) estimate that 67-97 per cent of melanoma in different populations is attributable to sun exposure. Recent epidemiological studies in the USA and Europe indicate that the development of moles (a lesion indicating the risk of melanoma) in children and the development of melanoma are influenced by short periods of intense UVB exposure (Autier et al., 2003, Fears et al. 2003). However, it is not impossible that exposure to UVA radiation plays a part in the development of melanoma (Armstrong, 2004).

Figure II-1 Ambient erythemal radiation and UVA (from dawn to 6.30 p.m. in clear skies during the month of maximum sunshine (Diffey and Elwood data, 1994)



Although complex interactions exist with host sensitivity factors and conduct (intermittent vs. continual exposure), it is likely that melanoma is basically caused by high levels of exposure to ultraviolet radiation. Gilchrest et al. (1999) have proposed a mechanism to explain the difference between induction of melanoma and squamous-cell carcinoma by ultraviolet radiation. According to this hypothesis, after ultraviolet radiation the most badly damaged keratinocytes undergo apoptosis, while the least damaged repair their DNA almost perfectly. The mutations are “fixed” in the basal layer of the epidermis, and can give rise to clonal expansion. Repeated exposure to low doses leads to accumulation of mutations, and gives rise to actinic keratosis and cancer. Conversely, in the melanocytes, a high initial dose of ultraviolet radiation causes substantial lesions but no apoptosis, the mutated melanocytes survive and divide (freckles and moles are clones of mutated melanocytes), and intermittent exposure to high doses gives rise to melanoma.

Effect of exposure to ultraviolet radiation on the tumoral progression of melanoma

Exposure to ultraviolet radiation may also play a part in the growth and tumoral progression of melanoma. Exposure to ultraviolet radiation cases local and systemic immunosuppression, which may be involved in promoting the growth of melanoma (for a review, see Kripke, 1994). Experimentally, local irradiation of mice increases the growth of a transplanted melanoma; this effect may be due to local induction of interleukin-10, and is not suppressed by a UVB filter (Donawho et al., 1994, Wolf et al., 1994). Moreover, UVB irradiation of

human melanoma lines increases their tumorogenicity and metastasis capacity in the nude mouse (Singh et al., 1995). Recent data also suggest that UV radiation may play a part in immunosuppression (Nghiem et al., 2001).

An odd phenomenon is the existence of seasonal variations in the incidence of melanoma, with the peak incidence in summer. These variations, which have been known for some 20 years, have been observed in several populations and in both hemispheres, and no clear explanation has yet been given (for a review, see Doré and Boniol, 2004). It is possible that the peak incidence in summer is due to increased diagnosis in summer, when people wear fewer clothes and active screening campaigns are conducted in some countries; however, this peak incidence has been observed in families at high risk of melanoma monitored prospectively, and in Hawaii, where the climate and clothing do not change significantly during the year. Another explanation may be that increased intensity of ambient ultraviolet radiation promotes the last stages of malignant transformation. Several arguments militate in favour of this hypothesis (Doré and Boniol, 2004). Firstly, the extent of the seasonal variation in incidence of melanoma varies inversely with latitude, and therefore with greater exposure to ambient UV radiation. Secondly, there is no seasonal variation in the incidence of melanoma *in situ* (pre-invasive). Finally, the cases of melanoma diagnosed in summer show all stages of development, not only thin melanoma (which would correspond to an increase in early diagnosis), and analysis of the thickness of the melanomas diagnosed in Burgundy shows that those diagnosed in summer are significantly thicker (mean 1.99 mm ± 2.23; median 1.07) than those diagnosed in winter (mean 1.24 ± 1.79; median 0.7) (Boniol and Doré, 2004). No published study has yet analyzed the clinical evolution of melanoma according to the thickness of the initial tumour and the season of diagnosis.

Effect of exposure to ultraviolet radiation on mortality due to melanoma

Exposure to sunlight, and especially intermittent recreational exposure, is the main known risk factor for melanoma. However, it has been known for some 20 years that sun exposure can also affect the survival of melanoma patients. One of the first observations was made by Lemish et al. (1983), who demonstrated that survival increased with incidence in a number of populations, and suggested that melanoma could be biologically more benign if it occurred in association with a high level of ambient sun exposure. In fact, the incidence and survival rate of melanoma are positively associated in time and place (Armstrong, 2004). Two studies have demonstrated a possible association between melanoma survival rate and solar elastosis, a skin lesion indicating sun damage (Heenan et al., 1991, Barnhill et al., 1996). These findings suggest that sun exposure may increase the melanoma survival rate, but may also be explained by an association between incidence and early detection of melanoma. A recent study of very high quality (based on 528 cases identified by a register and followed up for an average of 5 years) evaluated the association between screening measures, solar elastosis and risk of death. Multivariate analysis, which took account of individual variables, demographics, sun exposure, screening, and the clinical variables of the tumour, showed that sun exposure is associated with increased survival (Berwick et al., 2005). The mechanism of this effect is not known, but it illustrates the possibility that several pathways exist in the malignant transformation of melanocytes (Whiteman et al., 2003, Rivers, 2004). It has been suggested that this effect may be mediated by vitamin D, the antiproliferative and proapoptotic effects of $1,25(OH)_2D_3$ having been demonstrated in other cell models, but this is merely a plausible speculation at present. Another explanation might be that sun exposure induces the least aggressive melanomas, especially by inducing melanization and increasing the DNA repair capacity, which may reduce further mutations in a melanoma (Gilchrest et al., 1999).

Other cancers

A number of ecological studies have suggested that sun exposure is liable to interfere with the incidence or mortality rate of some types of cancer, especially breast, colon, and prostate cancer and lymphomas.

In the USA, an exploratory case-control study of cancer death certificates registered in 24 States between 1984 and 1995 demonstrated that residential sun exposure is negatively and significantly associated with mortality from breast, ovarian, colon and prostate cancer. Breast and colon cancer were also negatively associated with occupational sun exposure (Freedman et al., 2002).

A positive association between latitude of residence and mortality from prostate cancer has been interpreted as indicating that ultraviolet radiation may protect against the development of this type of cancer (Hanchette and Schwartz, 1992). A case-control study has provided results compatible with this theory. Sunburn in childhood (OR = 0.18; 95 per cent CI 0.08-0.38), regular holidays abroad (OR = 0.41, 0.25-0.68) and sunbathing (OR = 0.83, 0.76-0.89) are associated with a reduced risk of prostate cancer, while low UV exposure is associated with increased risk (OR = 3.03, 1.59-5.78). Moreover, the cases in which UV exposure is lowest develop cancer at a younger age (median 67.7 years, Q1-Q3 61.5-74.6) than those in which UV exposure is greatest (72.1 years, Q1-Q3 67.5-76.4); p = 0.006 (Luscombe et al., 2001).

As regard malignant Non-Hodgkin Lymphoma (NHL), the data are contradictory (see Hughes et al., 2004, for a review). On the one hand, ecological studies have shown a geographical distribution and parallel time trends between NHL and skin cancers, a negative correlation between incidence of NHL and latitude in Europe, a positive correlation between incidence of NHL and regional levels of ultraviolet radiation in the UK and Wales, and an increased risk of NHL with emigration from the UK to Australia. On the other hand, the incidence and mortality rate of NHL increase with latitude and decline with the increase in ambient UV radiation in the USA. Moreover, the association between personal history of basal-cell or squamous-cell carcinoma, which may indicate a high level of sun exposure and the risk of NHL in cohorts of cancer registers, and a weak association between sensitivity to sunlight and individual risk of NHL, tend to support a causal association. However, two recent case-control studies in Australia (Hughes et al., 2004) and Scandinavia (Ekström Smedby et al., 2005) demonstrate an inverse correlation between sun exposure and risk of lymphoma. In both studies, the reduction in risk is around 30 per cent; however, in the Scandinavian study, the association with personal history of skin cancer persists.

The greatest caution is required when interpreting the results of these studies. In fact, studies based on mortality data may reflect the fact that the population of patients who die differs from the population of incident cases. For example, Freedman et al. (2002) observed a marked socioeconomic gradient for prostate cancer, whereas differences in socioeconomic status were usually weaker in other studies. The mechanisms involved in these apparently protective effects against UV exposure are unknown. The fact that a personal history of skin cancer proved to be a risk factor for lymphoma in the Scandinavian study may imply that another risk factor, such as deficiency in a specific DNA repair pathway, may be common to both types of cancer (Egan et al., 2005).

Solar ultraviolet radiation is a proven carcinogen in man. It is the main environmental cause of skin cancer and of melanoma, a tumour which contributes disproportionately to the mortality rate among young adults.

The rather surprising results referred to above consequently need to be confirmed by new studies which take full account of sun exposure, and supported by studies of the mechanisms involved. The importance of the potential public health consequences makes any use of these results premature.

Cataracts

Cataracts are the main type of eye damage associated with exposure to UV-B radiation. An association between sun exposure (especially solar UV-B radiation) and an increased risk of senile cataracts has long been suggested. However, the initial studies lacked precision in the evaluation of cataracts, and failed to distinguish between the different types of cataract. Most studies, with a few exceptions, have not evaluated the individual exposure of the eye to UV-B radiation, but used ambient levels or isolated behaviour. Ecological studies show that there are more cataracts in hot countries, but while the ambient levels of UVB radiation may vary by a factor of 3-4 from one part of the world to another, individual behaviour can change eye exposure by a factor of 20 at a given place.

The epidemiological arguments in favour of this association come from studies conducted in Australia, China, Tibet and the USA (see Taylor, 1994, for a review).

In the USA, the arguments are based on population studies (sailors from Maryland, Beaver Dam Eye Study) and analysis of the cataract surgery data from the Medicare programme (which constitutes the healthcare cover for nearly all the 30 million Americans aged 65 and over, and funds 85 per cent of the 1.3 million cataract removals performed every year). Analysis of the Medicare data, adjusted for age, sex, race and income, access to ophthalmologists and opticians and the cost of surgery, shows that the most important factor in individual risk of undergoing cataract surgery is the latitude of the place of residence. Latitude is directly correlated with the proportion of UV-B in solar radiation, as the angle of incidence of the sun determines the penetration of UV radiation into the atmosphere. The probability of cataract surgery in the USA increases by 3 per cent for each 1° reduction (towards the south) in latitude (Javitt and Taylor, 1994).

A study of 838 sailors (mean age, 53 years) working in Chesapeake Bay (Maryland) evaluated individual ocular exposure to UV-B and showed a definite correlation between UV-B exposure and the risk of cortical and posterior subcapsular cataracts (Taylor et al., 1988). Annual ocular exposure was calculated for each sailor from the age of 16 years by combining a detailed occupational history with local solar exposure measurements. Cataracts were evaluated in terms of type and severity by ophthalmological examination. Some degree of cortical cataracts was found in 111 sailors (13 per cent), and of nuclear cataracts in 229 sailors (27 per cent). Logistical regression showed that high cumulative levels of UV-B exposure significantly increases the risk of cortical cataracts (coefficient of regression 0.70). The doubled cumulative exposure increases the risk of cortical cataracts by a factor of 1.6 (95 per cent confidence interval: 1.01 to 2.64). The sailors whose mean annual exposure fell within the upper quartile presented a non-significantly increased risk factor of 3.30 (confidence interval: 0.90 to 9.97) compared with those whose exposure fell within the first quartile. The mean annual UV-B exposure of the sailors with cortical lens opacity was significantly higher

(by 21 per cent). No association was found between nuclear cataracts and UV-B or UV-A exposure.

Another population study has shown that exposure to UV-B radiation may be associated with the severity of lens opacity in men (Cruikshanks et al., 1992). The correlations between exposure to sun and solar UV radiation and the prevalence of lens opacity have been studied in the inhabitants of Beaver Dam, Wisconsin. People aged 43-84 were examined using a standardized photographic evaluation of lens opacity, and answered a questionnaire about their medical history and exposure to light. The results of this study, adjusted for other risk factors, show that men with the highest levels of ambient exposure to UV-B have a risk of suffering from severe cortical opacity 1.36 times greater than men whose exposure levels are lower. No association was found between nuclear sclerosis or posterior subcapsular opacity in men. Moreover, no association with UV-B exposure was found in women, who are at less risk of being exposed to UV-B radiation. The absence of any association in women, the group most liable to suffer from cortical opacity, suggests that other factors may be important in the pathogenesis of lens opacity.

In conclusion, there is sufficient experimental proof that exposure to artificial UV-B sources may cause cortical opacity in laboratory animals. There is limited evidence that exposure to solar UV-B radiation causes cortical opacity in man. Equally, there is limited evidence that exposure to solar UV-B radiation causes posterior subcapsular cataracts in man. The epidemiological data suggest that nuclear cataracts are not associated with exposure to solar UV-B radiation (Dolin, 1994).

II.4.3 II.4.3 Epidemiological studies – artificial UV radiation

Exposure to solaria

A UV tanning session corresponds to exposure of at least 2 SED. In practice, one session corresponds to approximately 1 MED, i.e. for phototype II = 3 SED, phototype III = 5 SED and phototype IV = 7 SED.
Taking account of the national incidence of skin cancer based on latitude, the increased risk of skin cancer based on the number of annual artificial UV tanning sessions over a 10-year period between the ages of 20 and 30 can be calculated as follows:

$$\textbf{Risk} = (\textbf{Annual dose of ultraviolet radiation})^{\beta}\ (\textbf{age})^{\alpha}$$

where:
α = numerical constant
β = biological amplification factor.

This calculation was established by the NRPB, and is based on studies by Fears et al., 1977, Slaper & Van der Leun, 1987, and Diffey, 1987. For details and tables, see Board Statement on Effects of Ultraviolet Radiation on Human Health and Health Effects from Ultraviolet Radiation, NRPB (1995).

Risk of skin cancer based on number of annual sessions in a 10-year period:
10 sessions: risk multiplied by 1.03
30 sessions: risk multiplied by 1.10
100 sessions: risk multiplied by 1.39
300 sessions: risk multiplied by 2.73.

Skin cancer

It has long been believed that exposure to the artificial UV radiation of solaria presented no great danger, especially as several epidemiological studies were unable to prove the existence of a high risk. However, in 2002, an American study showed that in users of artificial tanning, the risk of developing squamous-cell carcinoma was multiplied by 2.5, and the risk of developing basal-cell carcinoma was multiplied by 1.5 (Karagas et al., 2002). More recently, a cohort study conducted on 106,379 Norwegian and Swedish women, monitored for 8 years, showed that the risk of melanoma associated with the use of tanning devices at least once a month is multiplied by 1.5 (2.6 in the 20-29 age group) (Veierød et al., 2003).

Melanoma

Most epidemiological studies which have explored the correlation between exposure to tanning devices and skin cancer analyzed the correlation with melanoma. These studies were examined in two recent general reviews (Autier, 2004, and Young, 2004), and the older ones were analyzed in detail in a monograph by the International Cancer Research Centre (IARC, 1992).

Sun exposure is a known cause of melanoma. It may therefore be suspected that exposure to tanning devices can also be a risk factor, due to the emission spectrum and the similarity of use between this equipment and natural sun exposure (sunbathing). Several studies have shown a positive association between the use of artificial tanning and melanoma, sometimes dependent on the total dose received or the duration of exposure, but the methodological limitations inherent in case-control studies in particular make it difficult to establish a definite causal relationship (Swerdlow and Weinstock, 1998).

Table II-11 summarizes the main features and results of 13 case-control studies of the association between exposure to sunlamps and/or sunbeds and risk of melanoma.

Table II-11 Correlation between use of tanning devices and melanoma. Case-control studies

Reference	Country, year of publication	Type of study	Cases	Controls	% exposure of controls	Crude OR (95% CI)	Adjusted OR (95% CI)	Comments
Holman et al.	Australia, 1986	Population	511	511		1.1 (0.6 - 1.8)	-	Global exposure 9%
Swerdlow et al.	Scotland, 1988	Hospital	180	120	8.3	4.1 (0.8 - 20.3)	3.4 (0.6 - 20.3)	OR for duration of use: never vs > 1 yr. Adjusted for moles, hair and eye colour, phototype and sun exposure.
Østerlind et al.	Denmark, 1988	Population	474	926	18		0.7 (0.5 - 1.0)	Adjusted for age, sex, host factors and sun exposure
Mackie et al.	Scotland, 1989	Hospital	280	280		M 2.6 (0.9 - 7.3) F 1.5 (0.8 - 2.9)	M 1.3 (0.2 - 7.9) F 1.2 (0.5 - 3.0)	Adjusted for moles, freckles, sunburn, tropical residence and phototype.
Walter et al.	Ontario, Canada, 1990	Population	583	608	M 14 F 17	M 1.9 (1.2 -3.0) F 1.5 (0.99 - 2.1) M+F 1.6 (1.2 - 2.2)	-	Adjustment for age, moles, phototype and socioeconomic status does not change the results. Greater effect for lentigo maligna melanoma and lesions of face or extremities.
Garbe et al.	Germany, 1993	Hospital	856	705	7	1.0 (0.7 - 1.5)	1.5 (0.9 -2.4)	Adjusted for moles, hair colour, phototype and different recruitment centres.
Autier et al.	Germany, Belgium and France, 1994	Hospital	420	447	M 14 F 17	1.0 (0.7 - 1.3)	2.1 (0.8 - 5.4)	Adjusted for age, sex and holidays in the sun, with 10 hours' cumulative exposure and exposure that began before 1980.
Westerdahl et al.	Sweden, 1994	Population	400	640	25	-	1.3 (0.9 - 1.8)	Adjusted for sunburn, hair colour, moles, and sun exposure.
Holly et al.	California, USA, 1995	Population	452	930	38	0.9 (0.7 - 1.2)	-	Study conducted in 1981-86 among women age 25-59.
Chen et al.	Connecticut, USA, 1998	Population	624	512	M 16 F 22	1.3 (0.97 - 1.7)	1.1 (0.8 - 1.5)	Adjusted for age, sex, phototype and sun exposure.
Walter et. al.	Ontario, Canada, 1999	Population	583	608		-	Trunk 1.6 (1.1 – 2.3) Rest of body 1.5 (1.1 - 2.1)	Adjusted for age, sex and phototype.
Westerdahl et al.	Sweden, 2000	Population	567	913	M 33 F 57	-	1.8 (1.2 - 2.7)	Adjusted for moles, skin type and sunburn.
Bataille et al.	UK, 2004	Hospital	413	416	M 16 F 31	-	1.2 (0.8 - 1.7)	Adjusted for age and sex. Significant risk among fair-skinned young people (OR = 2.7; (1.7 – 6.1), adjusted for sun exposure)

M = male, F = female

Eight case-control studies have failed to show any correlation between exposure to tanning devices and risk of melanoma. The first studies of melanoma, conducted in Canada (Gallagher et al., 1986 – not included in table), Australia (Holman et al., 1986) and Italy (Zanetti et al., 1988 – not included in table), which were published in the second half of the 1980s, did not show any correlation with the use of tanning devices. The Danish study by Osterlind et al. (1988) also showed no correlation, nor did a German study (Garbe et al. 1993). A hospital case-control study conducted in Scotland showed a non-significant increase in risk associated with an exposure period of over one year (Swerdlow et al., 1988). Another hospital study conducted in Scotland showed a low, non-significant increase in risk (Mackie et al. 1989). A study conducted on women aged 25-56 in the San Francisco Bay area, published in 1995 but conducted ten years earlier, between 1981 and 1986, did not show any correlation with superficial spreading melanoma or nodular melanoma. However, it should be noted that in the studies conducted around 20 years ago, except in the study by Holly et al., the rate of use of artificial tanning in the population was very low: from 7 per cent in Germany to 18 per cent in Denmark.

Six more detailed case-control studies, which took account of constitutional factors and natural solar exposure, show a positive association between exposure to tanning devices and the risk of melanoma.

- A case-control study of 583 cases and 608 controls, recruited from the population of Southern Ontario, Canada (Walter et al., 1990), showed a significant association (OR=1-6; 95 per cent CI (1.2 - 2.2)), which is more marked for men (OR=1.9; (1.2 - 3.0)) than for women OR = 1.5; (0.99 - 2.1), trend not significant). The age-adjusted cumulative exposure rates show a significantly increased risk trend, based on duration of exposure among both men and women. A new analysis of the study has confirmed this significant association between exposure to tanning devices and melanoma risk (Walter et al., 1999).
- In a hospital case-control study conducted in Belgium and France, and based on a register in Germany (Autier et al. 1994), the risk of melanoma was increased by exposure for a cumulative duration of 10 hours or more which began 10 years before the diagnosis of melanoma (OR = 2.7; (1.1 - 7.8), after multiple adjustments OR = 2.1; (0.8 - 5.4), same trend, but not significant), and greatly increased among people who had accumulated 10 hours or more of exposure for tanning purposes and suffered skin burns (OR = 9.0; (2.1 – 38.6)). When adjusted for a variety of factors, including number of weeks' holiday in the sun, this risk persists (OR = 7.4; (1.7 – 32.3)). The risk is therefore concentrated in people who manifest "risky" behaviour in relation to UV sources.
- Two case-control studies relating to 400 cases and 640 controls, and to 571 cases and 913 controls, recruited from among the population of Southern Sweden in 1988-1990 and 1995-1997, were published by the same team in 1994 and 2000 (Westerdahl et al., 1994 and 2000). These two studies support the theory that the use of tanning devices is a risk factor for melanoma. In the first study, the risk associated with use of this equipment was found not to be significant (OR = 1.3; (95 per cent CI 0.9 - 1.8)); however, the risk was significantly increased by 10 annual exposure sessions (OR = 1.8), and much higher in patients under 30 years old (OR = 7.7 for 10 sessions vs. none). In the latest study, after adjustment for host factors and sun exposure, the risk was significant for regular use (OR = 1.8; (CI 1.2 - 2.7)). The risk is associated with frequency of use and number of sessions, with a dose-response relationship up to a total of 250 sessions. Analysis by age groups shows that the highest adjusted risk is observed for regular use among people under 36 years old (OR = 8.1; (1.3 – 49.5)).

- A non-significant increase in the risk of melanoma (OR = 1.1; (CI 0.8 – 1.5) after adjustment) with the use of tanning devices was reported in a study of 624 cases and 512 controls recruited among the population of Connecticut, USA (Chen et al., 1998). However, in that study, the risk was found to be significant for home use, but not for use of commercial installations, and appeared particularly high for at least two different types of equipment (OR = 3.5; (CI 1.3 – 9.1) after adjustment).
- Finally, a hospital case-control study of 413 cases and 416 controls recruited in the UK did not show any significant increase in risk associated with the use of a solarium (OR = 1.2; (CI 0.8 – 1.7) after adjustment for age and sex). Conversely, this risk proved significant in fair-skinned young people (OR = 2.7; (CI 1.7 – 6.1) after adjustment for sun exposure). It is not impossible that in this study, the 7-year delay between exposure to the solarium and diagnosis of melanoma led to under-estimation of the long-term risk (Bataille et al., 2004).

In these studies, the rate of use of tanning devices by the control population is higher than in the first studies conducted before 1990. This rate ranged from 14 per cent in men in Canada and Europe to 57 per cent in women in Sweden. Use increased during the 1990s, and in the two studies conducted on the same population in Sweden in 1988-1990 and 1995-1997, the exposure rate practically doubled in 7 years.

All these case-control studies suggest the existence of a correlation between the use of tanning devices and the risk of melanoma, but although some of them show a more marked risk in some age groups and phototypes, it is difficult to draw any final conclusions. In practice, case-control studies suffer from a number of methodological limitations. Firstly, they do not constitute the ideal method of demonstrating an increase in relative risk if the relative risk is low (between 1.0 and < 2). Secondly, the answers given by melanoma patients about their exposure may be biased by the fact that they knew their diagnosis at the time of the interview. This interview bias may lead patients to minimize their exposure, but even the controls, knowing the risks of the recorded exposure, may also unconsciously bias their responses ("differential misclassification"). Finally, the selection of controls may lead to the inclusion of persons whose conduct differs from that of the general population (selection bias). Such biases are liable to have influenced the results of studies like that of Holly et al. (1995), in which sun exposure did not appear as a risk factor, and a multicentric European study conducted in 1999-2001 on 597 cases and 622 controls, currently in press. In that study, the use of tanning devices was the highest ever recorded (DeVries et al., 2002); the host factors (such as skin and moles) were found as expected, but sun exposure did not emerge as a risk factor (Bataille et al., submitted).

The preferable method for calculating a low relative risk is the longitudinal cohort study. In this type of study, exposures are recorded before the diagnosis, and this recording is less subject to interview bias. Moreover, a prospective cohort study relating to a large number of individuals is far more powerful than a case-control study, and therefore more appropriate to demonstrate the existence of a moderately high relative risk.

A prospective cohort study of this kind was recently published (Veierød et al., 2003), and is summarized in Table II-12. 106,379 women aged 30-50 at the time of their inclusion in the cohort in 1990-1991 were recruited in Norway and Sweden, in the Uppsala region, and monitored for 8.1 years on average; this represents a cohort of 866,668 person years of observation. During the monitoring of the cohort, 187 cases of melanoma were diagnosed in the cohort. The results of this study, adjusted for host factors and sun exposure, provide the

most convincing arguments for a causal relationship between melanoma and exposure to tanning devices. The study shows a significant increase in relative risk of melanoma (RR = 1.6; (1.04 - 2.3)) among 18 per cent of women who reported using a solarium at least once a month, at an age of between 10 and 39 years. The relative risk is highest for women aged 20-29 who are exposed at least once a month, (RR = 2.6; (1.5 - 4.5)).

Table II-12 Relative risk of cutaneous melanoma depending on solarium use. Summary of results of a prospective cohort study of 106,379 women aged 30 to 50 years, monitored for 8 years (Veierød et al., 2003)

Use of tanning devices and age when used	Frequency Number (%)		Number of cases	Multivariate RR* (95% CI)
10-19 years				
Never	84,182	(98)	152	1
Rarely or ≥ once per month	1,665	(2)	4	1.5 (0.5 – 4.1)
20-29 years				
Never	71,133	(80)	123	1
Rarely	11,618	(13)	19	1.1 (0.7 – 1.9)
≥ once per month	6,391	(7)	18	**2.6 (1.5 – 4.5)**
30-39 years				
Never	44,338	(50)	78	1
Rarely	28,383	(32)	51	0.9 (0.6 – 1.3)
≥ once per month	15,169	(17)	36	1.4 (0.9 – 2.2)
40-49 years				
Never	17,345	(42)	27	1
Rarely	14,514	(35)	33	1.4 (0.8 – 2.3)
≥ once per month	9,550	(23)	22	1.7 (0.9 – 3.0)
10-39 years (combined)				
Never/rarely	65,239	(82)	111	1
≥ once per month	14,377	(18)	34	**1.6 (1.04 – 2.3)**

*Poisson regression. Multivariate models include age, area of residence, hair colour, number of sunburns and the annual number of weeks of summer holiday.

A recently published meta-analysis, which brings together the data from nine case-control studies and from the cohort study by Veierød et al. (2003), found a positive association between exposure to tanning devices and the risk of melanoma, and estimated a significant overall risk level (OR = 1.25; (1.05 – 1.49)), with substantial heterogeneity. Evaluation of the exposure criteria “first exposure as young adult” (five studies) and “longest period or greatest frequency of exposure” (six studies) showed a significant increase in risk (OR = 1.7; (1.3 – 2.2), and OR = 1.6; (1.2 – 2.1), respectively), with no marked heterogeneity. Although it is not possible to determine precisely how much the use of tanning devices contributes to the individual’s risk of melanoma, it seems clear that even low use of such equipment increases this risk. Moreover, the risk increases with the latency period, and the length of time such devices are used is positively correlated to the risk level (Gallagher et al., 2005).

To sum up, the epidemiological studies, specifically a meta-analysis and a cohort study, show that the use of tanning devices increases the risk of cutaneous melanoma by a factor of 1.25 to 1.50. This risk increases with the frequency and duration of utilisation and is more marked when the person exposed is a young adult. It should be noted that a moderate but significant increase in a given risk can cause a large increase in the number of patients, depending on the frequency of use in the population – an important point at a time when artificial tanning is becoming increasingly popular.

Basal-cell and squamous-cell cancers

A number of case studies have linked exposure to artificial UV radiation to skin cancer, but very few case-control studies have explored the relationship between exposure to tanning devices and the risk of basal-cell and squamous-cell skin cancers.

In the early and then in the late 1980s, two hospital-based case-control studies conducted in Ireland showed no relationship between the use of tanning devices and the risk of skin cancer. In the studies of both O'Loughlin et al. (1985) and Herity et al. (1989), fewer cases than control subjects reported having used sunlamps or sunbeds (not significant).

A case-control study of 306 cases of squamous-cell carcinomas diagnosed in 1977-78 in 12 hospitals in the Montreal area, each case being matched with two controls from the same hospital, showed a positive association with the use of a sunlamp (OR = 13.4; (1.4 – 130.5) after adjustment for hereditary factors and exposure to sunlight. It should be noted, however, that this study was conducted by post, and that the response rate was low, at about 30 per cent of both cases and controls (Aubry and MacGibbon, 1985).

Another case-control study in Canada, conducted among male subjects in the province of Alberta, studied 226 cases of basal-cell cancer, 186 cases of squamous-cell cancer and 406 population control subjects. It showed no significant increase in risk for exposure to various types of non-solar UV sources after adjustment for host factors (OR = 1.2; (0.7 – 2.2), and OR = 1.4; 0.7 – 2.7), respectively) (Bajdik et al., 1996). Most basal-cell cancers in patients under 40 years of age are observed among women.

A recent study examined risk factors among 30 women patients and 30 matched controls. Although the patients' average total exposure to tanning devices was twice that of the controls (152.2 sessions versus 83.1), this difference is not significant (Boyd et al., 2002).

The only meaningful results are the findings of a case-control population study of 603 cases of basal-cell cancer and 293 cases of squamous-cell cancer, all residing in the state of New Hampshire (USA), and 540 control subjects (Karagas et al., 2002). In this study, 78 per cent of cases and 66 per cent of controls responded, and more of the subjects had used tanning devices, with utilization rates ranging from 9.2 per cent (male controls) to 28.4 per cent (female cases). The risks of basal-cell and squamous-cell cancer were significant (OR = 1.5; (1.1 – 2.1), and OR = 2.5; (1.7 – 3.8), respectively). Adjustment for various risk factors does not change the results. As in the case of melanomas, the risks increase when the first exposure occurred at a younger age. These results suggest that the use of tanning devices is a risk factor for non-melanoma skin cancers.

Concern in the scientific and medical community over the increasing use of sunbeds

In recent years, the scientific and medical community has expressed its concern over the increasing use of sunbeds.

As early as the late 1980s, the Photobiology Task Force of the American Academy of Dermatology and the British Photodermatology Group recommended that cosmetic tanning in sunbeds be discouraged (Bickers et al., 1985; Diffey et al., 1990).

In March 1996, France's Conseil Supérieur d'Hygiène Publique (Higher Public Health Council) issued an opinion recommending, among other things, that any reference to any beneficial health effect whatsoever be prohibited in advertising for such equipment and that information and warnings for users be mandatory (Conseil Supérieur d'Hygiène Publique de France, 1996; Doré et al., 1997).

More recently, two reports from France's National Academy of Medicine called attention to the risks of intentional exposure to artificial UV radiation and requested the prohibition of tanning in sunbeds (Tubiana and Rouessé, 2004; Bazex, 2003).

Dermatologists in the United States and Canada have also requested that tanning booths be prohibited.

In the United Kingdom, Cancer Research UK and the Sunbed Association held a joint meeting in 2004 to draw up a code of good practice.

Very recently, the radiation safety and health authorities in the five Nordic countries (Finland, Sweden, Norway, Denmark and Iceland) issued a joint opinion discouraging the use of sunbeds for non-medical purposes and warning citizens, particularly minors, of the risks of skin cancer. The five Nordic countries requested that the European Union place a stricter limit on the power of tanning devices.
http://www.sst.dk/upload/forebyggelse/cff/sol_hudkraeft/nordic_sunbed_position.pdf.

II.4.4 Other effects of UV radiation

Effects of UV radiation on skin aging

Little is known about the skin condition of the populations of the industrialized countries, even though, in terms of public health, skin pathologies are responsible for major morbid phenomena. Chronic exposure to sunlight, or to other environmental factors such as cigarette smoke, frequently has repercussions on the skin, commonly known as photo-aging, that vary with anatomical location, total exposure time and the individual's phototype. A French study (Malvy et al., 2000) was conducted to determine the reference values of skin condition markers in adult French subjects and to assess the relationship between skin photo-aging markers and behavioural and environmental factors. This research was conducted as part of the SU.VI.MAX study described above (see the section on skin types).

A cross-sectional analysis was conducted in 1995 on a sub-sample of 6,663 subjects (3,057 women and 3,606 men), from 45 to 60 years of age at the time of their inclusion in the SU.VI.MAX cohort. The total exposure to sunlight was estimated using a self-evaluated scale with four levels ("How would you describe the extent to which your skin has been exposed to sunlight during your entire lifetime: not at all, slightly, moderately or highly exposed?"). The phototype was determined by medical examination using the classification proposed by Césarini (Césarini, 1977). Skin photo-aging was measured using the photographic scale of Larnier et al. (Larnier et al., 1994), a six-level scale, each level being defined by three photographs to illustrate the diversity and range of features. The information on photo-aging was analyzed as a dichotomous variable (slight to moderate, or moderate/serious to very serious). First, a series of logistical regressions was conducted to test for the effect of each factor, adjusting for age; next, a multiple logistical regression model was constructed using the variables selected in the preceding stage. Separate analyses were carried out for men and women.

Men and women belonging to the same age groups show comparable rates of prevalence of photo-aging. Definite photo-aging of the skin was found in 1,194 women (39 per cent), 22 per cent in the 45-49 age group, 36 per cent in the 50-54 age group and 42 per cent in the 55-60 age group; and in 1,450 men (40 per cent), 17 per cent in the 45-49 age group, 38 per cent in the 50-54 age group and 45 per cent in the 55-60 age group. The self-evaluations of exposure to sunlight were similar for the two sexes and were found to be linked to phototype (percentage of subjects stating that they had been highly exposed to sunlight during their lives: phototype I and II, 7 per cent; IIIa, 7 per cent; IIIb, 10 per cent; IV, 14 per cent; V and VI, 24 per cent).

After adjustment for body mass index, smoking and exposure to sunlight, the variables found to be significantly linked to definite photo-aging in women were age; menopause; geographical location, with an effect due to UV protection in the areas of southern France that receive the most sunlight; and skin phototype, with a more marked effect for the lighter phototypes (I and II). Smoking was found to have an impact for women, although it was barely significant statistically. No connection was found between the use of oral contraceptives and skin photo-aging. For men, it was found that age and region of residence had an impact, and that there was more marked photo-aging for the darkest phototypes (V and VI).

These results suggest that the prevalence of skin photo-aging in the overall adult French population is determined by age, sex, phototype, region of residence and, for women, by menopausal status. Women of phototypes IIIA, IIIB and IV faced a significantly lower risk of definite photo-aging than women of lighter phototypes (I and II). The reason might be that they have better natural protection against the effects of the UVA radiation in sunlight, or that they have protected themselves better when exposed to sunlight than women of phototypes I and II. In men, in contrast to what was observed for women, the relative risk of photo-aging was not significantly higher among the paler phototypes. Subjects with a phototype higher than IV show a risk of definite skin photo-aging three times higher, which could reflect differences in behaviour, with increased exposure among male subjects who have better natural protection but are given to neglecting protective measures. Thus, darker-skinned subjects will show photo-aging effects at a later age than lighter-skinned subjects. Photo-aging seems to be partly determined by host factors, such as the melanin level in the epidermis, which is taken into account in assessing phototypes.

The lack of the expected association between skin photo-aging and the self-evaluation of total exposure to sunlight during the subjects' lifetime is probably due to the inadequacy of the variable used to estimate exposure to sunlight. For both sexes, an unexpected connection was found between geographical location and skin photo-aging. As southern France is a region deemed to have a high level of ambient ultraviolet radiation, subjects who live there may have adopted the behaviour of protecting themselves from the sun. In conclusion, the findings of this study show a high frequency of skin photo-aging in a sample of French adults drawn from the general population. The high rates of prevalence of this condition suggest the influence of both host-specific determinants and determinants stemming from the host's environment and behaviour.

Photodermatitis

Photodermatitis is a general term for all skin diseases involving photosensitivity, i.e. in which the skin shows abnormal reactions to light.

The diagnosis of photodermatitis is based on the presence of lesions that appear predominantly on the face (forehead, cheekbones, nose and back of the neck), but are absent from the areas under the nostrils and chin as well as the eyelids. Lesions on the wrist and dorsum of the foot that leave the areas covered by a wristwatch and shoes untouched are also symptomatic. The lesions may either follow the pattern of a sunburn (phototoxic reactions) or be due to more polymorphous reactions (urticaria, eczema etc.).

Photobiological exploration is used to reproduce the lesions, specify the reaction mechanism and identify an agent or product that may be involved in the reaction. The equipment uses artificial UV sources, and the procedure consists in determination of the minimum erythema dose (MED), phototests (with the aim of reproducing the observed lesions by means of irradiation) and photopatch tests (which confirm the role of certain pharmacological agents in the appearance of lesions by reproducing them in the presence of the photosensitizing agent). Exploration of photodermatitis is supplemented by histological studies of the lesions, metabolic studies or biological tests (e.g. porphyrin assays).

The main types of photodermatitis may be classified in 5 sub-groups:

- dermatitis exacerbated by sunlight (lupus erythematosus, recurrent herpes labialis, acne etc.). These diseases also appear without the influence of light, which acts in such cases as a non-specific stimulant;
- photodermatitis due to exogenous photosensitizing agents (drugs, cosmetics, botanical substances etc.);
- photodermatitis due to photosensitivity connected to metabolic anomalies that lead to the accumulation of endogenously produced photosensitizing factors (porphyria, pellagra etc.);
- genetic and metabolic photodermatitis due to anomalies in the formation (albinism) or distribution of natural UV protection factors such as melanin (vitiligo), or to deficiencies in DNA repair systems (Xeroderma pigmentosum). These deficiencies are reflected by exaggerated sensitivity to sunlight with enhanced acute effects (sunburns that are disproportionately severe in relation to the quantity of light received) and, most importantly, an increased risk of cancer;
- idiopathic photodermatitis (polymorphous light eruptions, solar urticaria etc.). The nature of these reactions is not known.

Effects of UV radiation on the eye

In adults, the cornea of the eye absorbs all UVC and most UVB radiation. UVA radiation passes through the cornea and is absorbed by the crystalline lens. Visible light and infrared radiation reach the retina. The transmission of radiation by ocular media changes throughout a person's lifetime: the eyes of infants and children are particularly vulnerable to UV radiation, with a narrow transmission window at about 320 nm that closes at about 10 years of age. Transmission of blue light (400-500 nm) falls from 60-80 per cent in children to 20 per cent in subjects over 60 years of age. It is therefore important to protect the eyes beginning in early childhood.

The acute risk of ultraviolet radiation and visible light for the eye:

- Acute actinic keratoconjunctivitis:

This condition appears following unprotected exposure to sunlight (particularly when the sun's radiation are reflected by snow, sand or cement) or to artificial light such as that of welding arcs, high-pressure discharge lamps and sunbeds. The symptoms of "arc flash" and "snow blindness" are tearing, redness and intense pain in the eyes, difficulty in keeping them open in the presence of light (photophobia) and a feeling of having sand in one's eyes. A few seconds of exposure to intense UV radiation are enough to cause these lesions, but photokeratitis is characterized by a latency period that varies inversely to the severity of the exposure. This period generally ranges from 6 to 12 hours. The subject is then visually incapacitated for 6 to 24 hours and recovers 48 hours later. Unlike the skin, the ocular system does not develop a tolerance to repeated exposure to UV radiation.

- Acute solar retinopathy (Bacin, 2001):

The damage inflicted on the retina by UVA radiation has been amply demonstrated in research on animals. The alteration affects the visual receptor cells, whereas exposure to blue light damages instead the pigmented epithelium. The retina is considered to be six times more sensitive to UV radiation than to radiation in the visible spectrum such as blue light. Acute solar retinopathy occurs after looking at the sun (e.g. during observation of eclipses) or after prolonged exposure to sunlight without eye protection. Sources of intense artificial light such as welding arcs and some surgical microscopes can also damage the retina.

UV radiation can cause other lesions in some subjects in the long term:

- Cataracts:

The crystalline lens is a colourless, avascular, biconvex lens. A cataract is an opacification of the crystalline lens due to a change in its composition, with higher water content and, most importantly, denaturation of its constituent proteins. Epidemiological studies, some of which involved over 100,000 people, give reason to think that cataracts may be directly linked to UV exposure. This research demonstrated, among other things, that areas receiving considerable UV radiation show a high prevalence of cataracts (a detailed analysis of these epidemiological studies is given in section II.4.2 above, "Epidemiological studies – natural UV radiation"). Moreover, studies conducted on animal models and *in vivo* established an undeniable relationship between UV exposure and the appearance of cataracts. The mechanism through which cataracts occur is probably connected to photo-oxidation of aromatic amino acids, including tryptophan. The repercussions of UV-induced cataracts are considerable in terms of both blindness and the number of cataract operations performed.

- Senile macular degeneration (SMD):

This disease of the retina currently affects one of every four people in the 75-85 years age group. It causes partial but virtually incurable blindness by cutting out the centre of the field of vision. Repeated exposure to UV radiation may lead to SMD. SMD is a frequent cause of visual disability, and its social impact is projected to be even greater in the future, as the proportion of the French and European population likely to exhibit this pathology increases.

Lipofuscin, an aging pigment of the pigmented epithelium of the retina, accumulates throughout an individual's lifetime and might be responsible for both the malfunctioning of visual receptors and SMD. The release of retinal lipids during inflammatory reactions caused by exposure of the retina to sunlight also suggests that polyunsaturated fatty acids may be involved in light-induced lesions.

SMD is a degeneration of visual receptors and the pigmented epithelium. A form of this condition called "exudative" SMD is characterized also by the growth of vessels stemming from choroidal capillaries. Oxygen-reactive species are produced at the macula in large quantities under the effect of blue radiation (390-440 nm) as radiation is converted into an electric signal directed at the optical nerve. It has been amply demonstrated that when the macula is illuminated the oxidation metabolism is highly active and the oxidation defences come into play.

It has been shown that these defences often fall to the level of the retina or the blood in subjects with SMD. The proportion of carotenoid compounds, whose role in vision is well known, decreased, particularly in subjects who smoke, which is a recognized risk factor for the onset of SMD (Bonne, 2003). Therapeutic trials (oral supplements containing selenium versus placebos) showed the value of dietary supplementation in slowing the progression towards more serious forms of SMD. Various studies on radiation penetration have demonstrated that a significant proportion of ambient UVA and even sometimes UVB radiation are absorbed in the crystalline lens, and that the more dilated the pupil, the higher the proportion absorbed. This absorption causes a gradual clouding of the crystalline lens.

A recent epidemiological study (Tomany et al., 2004) of a cohort of over 6,000 individuals seems to establish a link between SMD and prolonged exposure to the sun (particular during

adolescence) and suggests that the risk is reduced by over 50 per cent if individuals protect their eyes by wearing sunglasses and hats, caps or visors.

It is thus essential, during sessions of exposure to artificial UV radiation with a high level of blue visible light, to wear goggles designed specifically to absorb all such radiation. Note that repeated surveys in various countries have shown that 40 per cent of tanning device users refused to wear such protective device for cosmetic reasons (avoiding “panda eyes”), despite the specific recommendations on this subject. The risks of later symptoms are apparently quite real.

III Behaviour and exposure[3]

III.1.1 Exposure to natural UV radiation

Measuring natural UV radiation of environmental origin

Ultraviolet (UV) radiation is the highest-energy radiation of the entire range of non-ionizing radiation emitted by the sun that reaches the earth's surface. For this reason, it has not only major biological effects on human beings, fauna and flora (skin cancers, cataracts, loss of vegetation, etc.) and chemical effects on the off-gases produced by human activity (production of tropospheric ozone and other toxic gases through photolysis). The energy from UV radiation that reaches the ground depends on latitude, with the maximum levels at the equator and the minimum levels at the poles. France is in an average position. The baseline publications in the literature are based on one-off measurement campaigns conducted in 1993 and have not been updated (Elwood et al., 1993).The stratospheric ozone layer, which absorbs a high proportion of short wavelengths, is a natural barrier that protects us in part from solar UV radiation; the thinning of this layer, which has been observed for several decades now, is thus likely to lead to increased UVB irradiation in the troposphere and at ground level (Henriksen et al., 1990; Jones, 1992). The climatic variations observed today also have a powerful effect on the amount of UV radiation reaching ground level, as they tend to change the duration of cloudy periods during which the sun's radiation are screened by clouds. In short, analysis of the impact of various active parameters on UV radiation (ozone, cloudiness, aerosol sprays, ground reflection factor) and of the effects of changes in these parameters over time is itself a broad, complex field of study.

The scale of the biological and photochemical consequences of variations in ground-level UV radiation from the sun has made the international scientific community aware of the need to develop a climatology of such radiation and to monitor long-term trends. This led to the establishment of an international network, the Network for Detection of Stratospheric Change (NDSC), and the formation of an ad hoc working group. The two French stations for measuring ground-level UV radiation, located at Lille-Villeneuve d'Ascq and Briançon-Villard St Pancrace, have been an integral part of this global network since 2001.

Measurements are taken fairly regularly in many countries, particularly in Europe. The European Union played an important role in the construction of a European network by providing financial support to instrument comparison campaigns and establishing a database at the Finnish Meteorological Institute (FMI) in Helsinki; these activities were conducted as part of the Scientific UV Data Management (SUVDAMA) project, which was followed by the European Database for Ultraviolet Radiation Climatology and Evaluation (EDUCE) programme. The two French stations send their data regularly to this database. At the same time, a project for satellite-based measurement of solar radiation (the SoDa programme) was developed starting in 1985.

Satellite observation

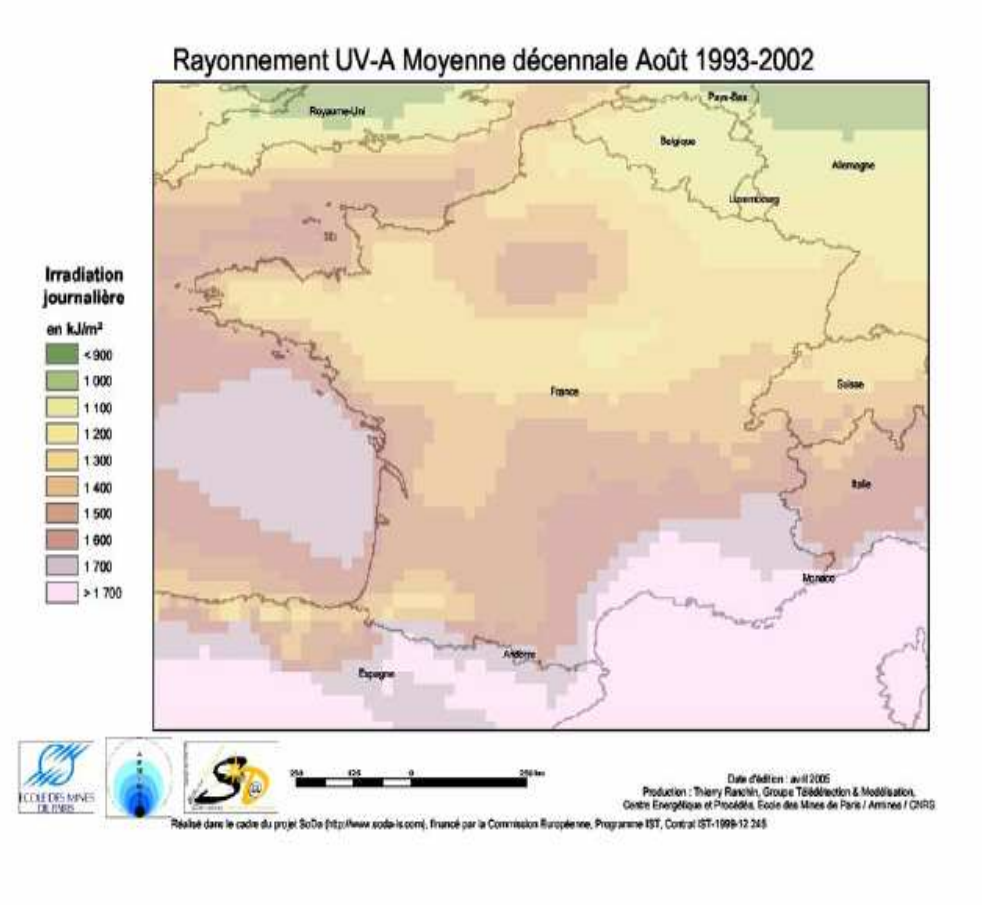
Since 1985, the SoDa programme (www.soda-is.com) has been using observations by meteorological satellites to measure the solar radiation received at ground level. Through the use of the proper algorithms, this makes it possible to estimate the shares of UVA, UVB and

[3] This section is drawn from the work of the InVS experts' group.

erythemal UV radiation. It thus provides a database comprising a time series of UV radiation data (daily, monthly and annual observations) for France's entire territory, divided into squares 5 km to a side. The advantage of this system is that its grid completely covers France's national territory and the ease of measurement it offers. As the archive is currently limited to 21 years, however, it does not allow calculation of variations in UV exposure in relation to climate change. An example of a UV exposure map for France is given below (Figure III-1).

Figure III-1: Example of geographical distribution of UV radiation (1993-2002 average)

Ten-year average UVA radiation, August 1993-2002



Royaume-Uni – United Kingdom; Belgique – Belgium; Pays-Bas – Netherlands; Luxembourg – Luxembourg; Allemagne – Germany; France – France; Suisse – Switzerland; Italie – Italy; Monaco – Monaco; Andorra – Andorra; Espagne – Spain.

Ground-level observation

Two stations in France are currently equipped with UV spectroradiometers, which are recalibrated regularly and have participated successfully in several European campaigns. These instruments record, at 30-minute intervals, the spectrum of total solar UV irradiance received at ground level in a horizontal plane.

The Lille-Villeneuve d'Ascq station, located in a low-lying urban, industrial area and attached to the Lille University of Science and Technology (USTL), has been equipped since 1997 with a UV spectroradiometer with a Jobin Yvon double monochromator; it has been in regular use since 1999.

The Briançon-Villard St Pancrace station, a site in a moderately high mountainous area (1,310 m) that belongs to the Centre Européen Médical et Bioclimatique de Recherche et d'Enseignement Universitaire – CEMBREU (European Medical and Bioclimatic Centre for Research and University Teaching) has two UV spectroradiometers. One of them is similar to that of the Lille station, while the other uses a Bentham double monochromator with similar characteristics. These instruments, which have been in operation since 1999, are managed by Joseph Fourier University in Grenoble. The use of two instruments, though it may seem redundant, makes it possible to avoid interruptions in measurement when one instrument needs recalibration or repair, and to validate the data through regular cross-checking.

These two stations for spectral measurement of solar UV radiation operate as a network. Their scientific purposes are as follows:

- to study the natural variability of this radiation and the various parameters that modulate it;
- to detect any long-term trends related, in particular, to human activity;
- to provide spectral UV data allowing validation of climatologies based on satellite observation;
- to make this data available to various communities of potential users (the medical community, biologists, photochemists, atmospheric chemists, etc.).

Sécurité Solaire data and the MOCAGE model: sequential monitoring of exposure based on meteorological satellites

The following information on Sécurité Solaire data and the MOCAGE model was obtained from P. Cesarini of the not-for-profit organization Sécurité Solaire (Solar Safety) and V.H. Puech of the French meteorological agency Météo France (http://www.ecmwf.int/research/EU_projects/GEMS/workshops/Dec_2003/8).

From 1994 to 1998, the not-for-profit organization Sécurité Solaire (Solar Safety), recognized as a WHO collaborating centre for the Intersun programme, took measurements of environmental UV radiation at stations located in several regions (Paris, Blagnac, Perpignan, Caen, Lille, Bordeaux, Nantes, Briançon, Font Romeu, Montpellier and Toulon). The instrument used was a broadband sensor providing a synthetic analysis of UV irradiation in the form of a UV index. The findings of these studies have neither been published nor been included in an official report; they are simply noted in Sécurité Solaire's report of activity.

Based on UV index data, cloudiness data and data on the chemical composition of the atmosphere, including ozone, as measured by meteorological satellites, a mathematical model of the correlation between the amount of sunlight and the chemical parameters was constructed so as to compute the UV index. The model, an application of the MOCAGE (MOdèle de Chimie Atmosphérique de Grande Echelle – Large-Scale Model of Atmospheric Chemistry) project, is now operational and is used for UV index forecasts, which are currently transmitted to the media by Sécurité Solaire. The model has national coverage and the data is

recorded in the form of forecasts. As we learned of the existence of this model and data only late in our survey, we were not able to identify any areas where the information from this system converges with or complements the data stemming from the other measurement systems described herein.

III.1.2 Human behaviour with respect to natural UV radiation: review of the French data

Considering the impact of intermittent UV exposure and the role of exposure during childhood, information on human behaviour with respect to UV radiation is very important in analyzing UV risk.

In one century, the behaviour of the populations of Western countries with respect to UV radiation has changed radically, from aversion to a strong affinity (Albert et al., 2002; Albert et al., 2003; Albert et al., 2003). This affinity for exposure to UV radiation typically takes the form of intermittent exposure, particularly in connection with leisure activities, owing to the increase in leisure time and the fact that it is easy to engage in leisure activities in countries that receive a great deal of sunshine, particularly during the winter. It is also linked to the use of sunbeds, the recreational aspect of which is both a selling point and an argument in favour of their development.

Most of the information available to date comes from studies of the populations of other Western countries (Australia, Canada, Great Britain, the Scandinavian countries), which also provide methodological principles and comparative data (Coogan et al., 2001; Godar, 2001; Godar et al., 2001; Godar et al., 2003; Sandby-Moller et al., 2004; Sandby-Moller et al., 2004; Thieden et al., 2000; Thieden et al., 2001; Thieden et al., 2004; Thieden et al., 2004). The French data is rather limited, but for this report we felt it would be useful to review this data.

The SU.VI.MAX cohort

The SU.VI.MAX cohort is a national cohort of volunteers participating in a controlled trial concerning absorption of a precise dose of food supplements (recommended doses of vitamins A, E and C, selenium and zinc) (Hercberg et al., 1998; Hercberg et al., 2004). The cohort consists of 12,741 subjects, at least 35 years of age on their inclusion in the cohort, recruited in 1994 and monitored for 8 years. The minimum age for inclusion in the cohort was 35 years for women and 45 years for men; the maximum age was 60.

Among the many studies of the SU.VI.MAX cohort, a self-administered questionnaire to study behaviour concerning solar exposure and protection was developed with a view to later estimation of this cohort's risk of photo-aging and the occurrence of skin pathologies related to different types of behaviour. The first part of the questionnaire dealt with the description of the skin phototype (Guinot et al., 2005) and habits regarding exposure to and protection from the sun during the preceding year; the second covered habits of exposure to sunlight, evaluated in terms of total exposure over the subject's lifetime. This questionnaire was sent to the 12,741 volunteers in the cohort in February 1997. Seventy per cent of the questionnaires were returned, and 91 per cent of these were usable. In all, the data for 4,825 women and 3,259 men were analyzed. An initial descriptive analysis yielded indicators summarizing exposure to and protection from the sun (Guinot et al., 2001); then, a classification of individuals according to their habits regarding solar exposure and protection was developed (Mauger et al., 2004).

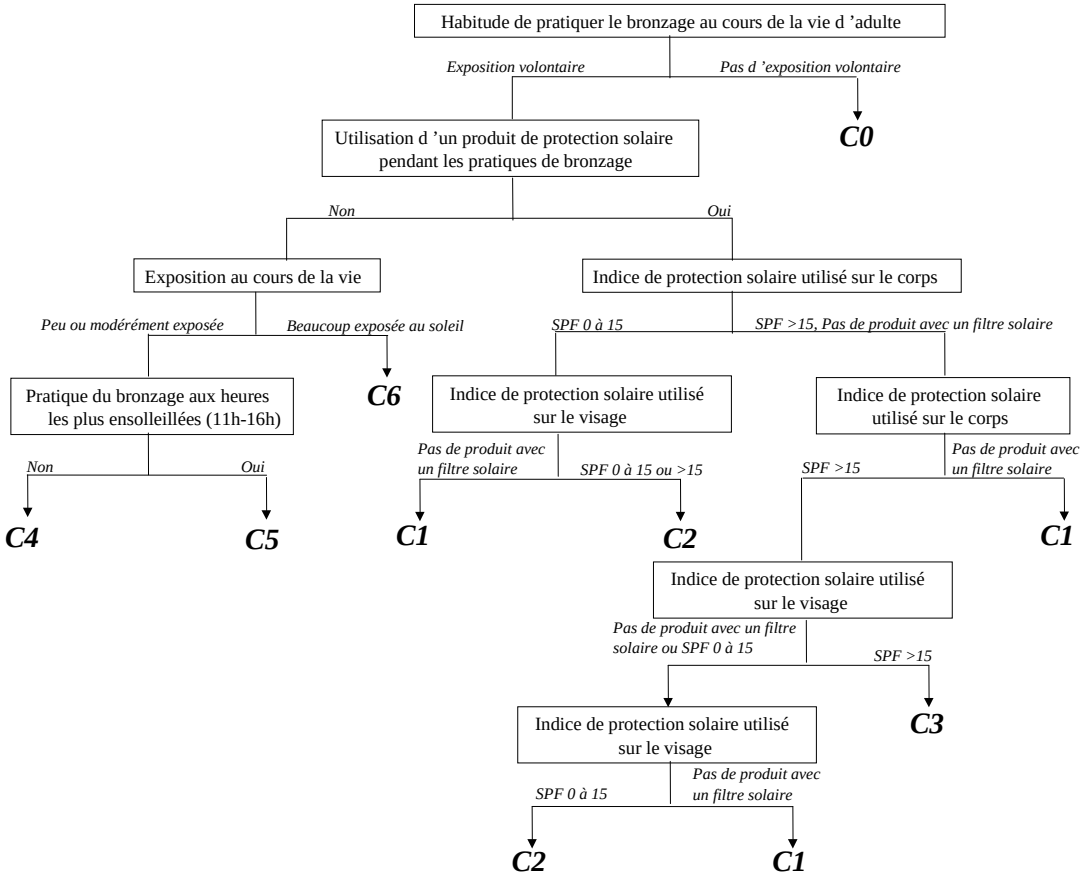
The research concerning a typology of behaviours was conducted by sex. Individuals who reported that they did not intentionally expose themselves to sunlight were considered to be in a class by themselves. Thereafter, a first analysis was performed for individuals having stated that they deliberately exposed themselves to sunlight and used sun protection products, and a second analysis for individuals having stated that they deliberately exposed themselves to sunlight and did not use sun protection products. The same analytical strategy was used for the two sub-samples: firstly, an analysis of the many correspondences found was performed in order to obtain an accurate summary of the information; secondly, an ascending hierarchical cluster analysis (Ward's method) was conducted to construct the classes; lastly, to make it easy to assign any individual to a class, a decision tree was constructed in order to determine decision-making rules based on a small number of questions (CART algorithm and Gini coefficient).

Table III-1: Exposure of women to sunlight (SU.VI.MAX study)

No deliberate exposure to sunlight during lifetime		C0, n=1,558
Deliberate exposure to sunlight and use of sun protection products	Sun protection without sunscreen. Moderate exposure.	C1, n=284
	Medium-strength sun protection. Intense exposure.	C2, n=1,364
	Strong sun protection. Moderate exposure.	C3, n=466
Deliberate exposure to sunlight without use of sun protection products	Moderate and prudent exposure.	C4, n=58
	Moderate and imprudent exposure.	C5, n=136
	Intense exposure.	C6, n=43

A decision tree based on six questions and ten decision-making rules was obtained (Figure III-2).

Figure III-2: Decision tree for women



Tanning habits during adult life

Deliberate exposure

No deliberate exposure

C0

Use of a sun protection product during tanning

No

Yes

Exposure during lifetime

Sun protection factor used on body

Little or moderate exposure

Extensive exposure

SPF 0-15

SPF > 15, no products with sunscreen

C6

Tanning during the hours of strongest sunlight (11 a.m.–4 p.m.)

Sun protection factor used on face

Sun protection factor used on body

No

Yes

No products with sunscreen

SPF 0-15 or > 15

SPF > 15

No products with sunscreen

C4

C5

C1

C2

C1

Sun protection factor used on face

No products with sunscreen or SPF 0-15

SPF > 15

C3

Sun protection factor used on face

SPF 0-15

No products with sunscreen

C2

C1

Table III-2: Exposure of men to sunlight (SU.VI.MAX study)

No deliberate exposure to sunlight during lifetime		C0, n=1,547
Deliberate exposure to sunlight and use of sun protection products	Sun protection without sunscreen. Many exposures	C1, n=209
	Medium-strength sun protection. Few exposures	C2, n=458
	Strong sun protection. Few exposures	C3, n=131
Deliberate exposure to sunlight without use of sun protection products	Few exposures	C4, n=293
	Many exposures	C5, n=118

A decision tree based on eight questions and eleven decision-making rules was obtained. The questions were the same as for women, with two additional questions: one on how important sunbathing was to the subject, the other on whether a sun protection product was used regularly the preceding year.

The limitation of this national cohort, from the standpoint of learning about UV exposure, is its demographic representativeness. The subjects studied belong exclusively to the generations from 1930 to 1960, with the age composition differing by sex, which makes it impossible to estimate more recent, generation-based changes in behaviour with respect to natural and artificial UV radiation. Moreover, the cohort was formed on the basis of voluntary involvement in a nutritional supplementation trial, which may introduce selection biases from the standpoint of social representativeness, and potentially from that of behaviour with respect to UV radiation.

Montpellier child study

A 1993 study, based on a self-administered questionnaire, of 573 children aged 3 to 15 in the Montpellier area (Vergnes et al., 1999) sought information on exposure to the sun during the summer of 1992. Children from junior secondary schools in "priority educational zones" and vocational secondary schools were excluded. The skin types of the sample are described. Eighty-five per cent of the children were light-skinned, and 15 per cent dark-skinned. Hair colour was light brown in 49 per cent of cases, blond or red in 40 per cent, black or dark brown in 11 per cent. Exposure to UV radiation during the summer was considerable, exceeding 6 hours per day in some cases, which for an entire summer amounts to 366 hours of median exposure. The proportion of children having suffered from a sunburn was 89 per cent. This study also examined the sun protection behaviour concerning protection from the sun (sunscreen use or wearing a t-shirt). The study showed that most of the recommended protective measures were not followed. This one-off study was not repeated, and it covered no other geographical areas. The exclusion of certain population categories for reasons of feasibility makes it difficult to generalize the study's conclusions.

Montpellier adult study

This national study, analyzed in 2001, was conducted during a randomized multicentric interventional trial for prevention and early diagnosis of skin cancer in health examination centres (Stoebner-Delbarre et al., 2001). The cohort consisted of a sample of 41,143 adults over 30 years of age residing in France and having had a periodic check-up in a health examination centre. The sample excluded people who unable to read French, blacks and Asians, and people who refused to participate in the study. In all, 33,021 people completed the self-administered questionnaire, which included items on awareness of the risks associated with exposure to the sun, attitudes, beliefs and behaviour regarding such exposure, and the social and demographic characteristics of the persons surveyed. Adults' attitudes with regard to exposure to the sun were analyzed using correspondences factorial analyses. This study mainly provided information on how informed the adult population is concerning exposure to the sun. It was not intended to collect information on exposure itself, nor to determine the time budget of those surveyed with respect to UV exposure.

III.1.3 Exposure to artificial UV radiation

The UV dosimetry[4] of a typical tanning session is known. One UV tanning session corresponds to an exposure of 2 standard erythema dose (SED) units. In fact, one session is equivalent to approximately one minimum erythema dose, i.e. 3 SED for skin type II, 5 SED for skin type III, 7 SED for skin type IV. There is very little data on use of artificial UV radiation, however, since only two general population studies have been conducted.

International data

The use of sunbeds is growing rapidly in the developed countries today, particularly in Northern Europe but also in France. In the United States, it was estimated ten years ago that approximately a million people a day visited a tanning salon and that the tanning industry generated annual turnover of over $1 billion (De Leo, 1994).

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[4] The minimum erythema dose (MED) is defined as the amount of ultraviolet radiation, regardless of wavelength, needed to cause a light sunburn with clearly defined edges 16 to 24 hours after exposure to the sun. This amount varies with subjects' sensitivity to sunlight. This dose was used to construct the reference erythemal efficiency spectrum (CIE, 1987), which is used as the basis for calculating the erythemal yield of all sources of UV radiation. The effective irradiation of UV appliances must comply with the values prescribed in the table defining types of UV sources.

The erythemal efficiency of each wavelength is weighted according to the erythemal efficiency curve and normalized to 298 nm. The erythemal effectiveness curve may be expressed in terms of mathematical functions:

$EE(\lambda) = 1.0$ $(250 \leq \lambda \leq 298 \text{ nm})$

$EE(\lambda) = 10^{0.094\,(298-\lambda)}$ $(298 \leq \lambda \leq 328 \text{ nm})$

$EE(\lambda) = 10^{0.015\,(140-\lambda)}$ $(328 \leq \lambda \leq 400 \text{ nm})$

In 1997, the CIE recommended the universal use of an erythemal unit, the standard erythema dose (SED), having the value of 10 mJ/cm^{-2} (100 J/m^{-2}) normalized in accordance with the erythemal efficiency curve to 298 nm. This unit will be used to define the erythemal power of all UV sources.

A 1991 case-control study by the Melanoma group of the EORTC[5] in five centres in Germany, Belgium and France showed that 19 per cent of all control subjects had used sunlamps or sunbeds. Use of this equipment was more frequent in Germany (25.3 per cent) than in Belgium (19.9 per cent) and France (6.4 per cent), and was more frequent among young people (31 per cent of the under-40 age group) having a high socio-economic level and low tanning capacity (27 per cent of blond and 30.8 per cent of red-haired people). Eighty-four per cent of the exposures reported had begun after 1979 (Autier et al., 1994).
Another case-control study by the same group, of the risk of melanoma, conducted from 1998 to 2000 in Sweden, the Netherlands, the United Kingdom, Belgium and France among subjects under 50 years of age (the average age of the control subjects was 37 years), showed that 57 per cent of the control subjects used artificial tanning at least once, with the highest rates of use found in Sweden (87 per cent). Such exposure was more frequent among women (61 per cent) than men (43 per cent). This new study showed the very high prevalence of exposure in the northern countries (Sweden and the Netherlands) and that the use of tanning devices is becoming more frequent among men and young people, with considerable variation from one country to another: among men, rates of exposure were highest in Sweden (78 per cent) and the Netherlands (60 per cent), but of only 39 per cent in the United Kingdom and 13 per cent in France. Exposure before the age of 15 years was reported by 3 per cent of all control subjects, but the figure for Sweden was 20 per cent. The average age of first exposure was 20 years in Sweden, 23 in the United Kingdom and 27 in France (Bataille et al., 2005).
This considerable increase in the use of tanning devices in Sweden is confirmed by two studies conducted in the same region in southern Sweden in 1988-90 and in 1995-97. In 1988-90, 46 per cent of individuals under 30 years of age had used sunlamps or a solarium at least once in their lifetime (56 per cent of women and 12 per cent of men, these percentages being higher in the 15-24 age group), while this proportion was only 24 per cent in the over-30 age group (31 per cent of women and 16 per cent of men) (Westerdahl et al., 1994). After 1995, the percentage of the 16- to 80-year-old population using such equipment was 41 per cent, but 70 per cent of women and 50 per cent of men from 18 to 50 years of age reported the use of a solarium (Westerdahl et al., 2000).

Since 1989, 13 studies have examined the use of tanning devices by children and adolescents (11-19 years of age), primarily in Norway, Sweden and the United States. All of these studies show frequent use by children and adolescents, sometimes at very young ages (see Lazovich and Forster, 2005, for a review). According to the most recent studies, 30 per cent of Swedish adolescents (13-19 years) and 24 per cent of US adolescents stated that they used tanning devices, and 7.5 per cent and 11.78 per cent respectively reported frequent use (ten or more times a year). Very few countries have adopted regulations on tanning booths, and where such regulations do exist, they often say nothing about whether minors should be allowed to use them. According to a recent study, France is the only country with a regulation that prohibits access by minors (Dellavalle et al., 2003).

[5] European Organization for Research on Treatment of Cancer.

French data

Information on exposure to artificial UV radiation is highly fragmented in France. In practice, only two studies estimate such exposure, and sources of information provided by the tanning industry are very limited.
The linkage between intentional and unintentional exposure has never been explored in a sample of the French population.

The SU.VI.MAX study

In 2001, a self-administered questionnaire on behaviour with respect to solar exposure and protection was sent specifically to the 12,741 French adult volunteers in the SU.VI.MAX cohort. Over 60 per cent of the questionnaires were returned, and 97 per cent of these were usable. This analysis, conducted separately for each sex, sought to describe the use of artificial tanning devices over the subjects' lifetimes.

Of the 7,359 individuals who completed the questionnaire, 1,179 (16 per cent) – 953 women (22 per cent) and 226 men (8 per cent) – reported that they had used tanning devices during their lifetimes. In both sexes, the skin phototype distribution among users was similar to that among non-users.

Forty-four per cent of women having used such devices belong to the age group that was youngest at the time of inclusion in the cohort (35-44 years), as against 33 per cent of women who had not used them (for men, no data is available concerning this age group).

Table III-3: Use of tanning devices during lifetime (SU.VI.MAX study)

	Women		Men	
Use of tanning devices during lifetime	Users 953 (22%)	Non-users	Users 226 (8%)	Non-users
Regular use	7%	-	6%	-
Use ≥ five years	10%	-	10%	-
Residence in northern France or Ile-de-France region	48%	39%	45%	36%
Practice of tanning in sunlight between 11 a.m. and 4 p.m. during lifetime	56%	37%	53%	38%
Regular application of sun protection products while tanning	39%	24%	17%	7%
Gradual exposure of skin to sun	54%	43%	53%	38%
Practice of naturism during lifetime	13%	6%	19%	8%
Sunburn in adulthood	93%	88%	93%	89%
Very or extremely extensive practice of tanning	37%	20%	26%	11%

Furthermore, knowledge of the risks associated with exposure to the sun seems as high among users of tanning devices as among non-users, regardless of sex. More than 95 per cent of users have heard of melanomas and know that sunburn can have serious consequences for their skin.

The reasons given for use of artificial tanning devices are as follows:

Table III-4: Reasons given for use of artificial tanning devices (SU.VI.MAX study)

Cosmetic reasons	35%
Preparing skin for exposure to sun	34%
Medical reasons (acne, psoriasis, vitiligo, rickets, vitamin D deficiency and allergies)	10%
Trying out the equipment because it was available or owing to curiosity	6%
For mental or physical well-being	2%
To avoid exposure to natural UV radiation	1%
Other reasons	2%
No reason given	23%

A link was found with skin phototype (Fitzpatrick's classification): individuals with the lightest skin types reported more often that they used an artificial tanning device to prepare their skin for exposure to the sun.

Adult cohort

In the Montpellier adult study, 2 per cent of subjects reported that they use sunbeds (Stoebner-Delbarre et al., 2001). There is no obvious methodological explanation for the scale of the discrepancies between these results. The reason probably lies in the diversity of behaviour with respect to UV radiation, particularly artificial UV radiation, but this aspect needs to be measured more accurately.

Economic data

Not enough economic data are available on the sector for analytical monitoring of the tanning business, which according to its practitioners is growing (personal communication from E. Boutet, Chairman of France's Syndicat National des Professionnels du Bronzage en Cabine – National Union of Tanning Booth Operators). The number of installed tanning devices can be obtained from declarations made to the prefects [the Direction Départemental des Affaires Sanitaires et Sociales – DDASS (Department of Health and Social Affairs) and Direction Départementale de la Concurrence, de la Consommation et de la Répression des Fraudes –DDCCRF (Department for Competition, Consumer Affairs and Fraud Control) of each territorial department], but as such declarations are voluntary, the number of devices may be understated. Furthermore, in addition to the mere number of devices installed, information is needed on their activity and how much they are used.

Reasons for tanning – Physiological effects of UV exposure

Research on the reasons why people want to be tanned have shown the importance of psychological and sociological motivations among teenagers: they want a positive image in the eyes of others (for a review, see Young, 2004, and Lazovich and Forster, 2005).

More recently, research studies have sought to identify more physiological effects. One of the main reasons given by university students who visit tanning salons is the relaxing effect of UV sessions (Knight et al., 2002). This effect might be due to the release of the many neuroendocrine mediators produced in the skin in response to UV irradiation (Gilchrest et al., 1996). Although no increase in the serum concentrations of opioid peptides (beta-endorphin and metenkephalin) was detected after exposure to tanning devices (Gambichler et al., 2002), it has recently been demonstrated that exposure to tanning devices does cause a real physiological effect (reinforcing stimulus). Fourteen young adults (one man and thirteen women from 22 to 32 years of age) who habitually use tanning devices were exposed twice a week for six weeks, during the same session, to two identical tanning devices equipped with filters transparent to visible light and infrared, one of which was transparent to UV radiation (4 per cent UVB, 96 per cent UVA) and the other opaque to UV radiation. The two filters were indistinguishable. At the end of each week, subjects were offered a free session with the device of their choice. Of the 12 participants who took advantage of the offer at least once, 11 chose each time the device that emitted UV radiation; in all, this device was selected 39 times out of 41 (Feldman et al., 2004).

III.1.4 Conclusions of studies on human behaviour with respect to UV radiation in French population groups

To date, there are no general studies of the French population, covering all age groups, on human behaviour regarding natural or artificial UV radiation. The studies that have been conducted have served to validate the questionnaires and a methodology. The behaviour of teenagers and young adults, however, is entirely beyond the scope of these studies, although these age groups are a commercial target for tanning booth businesses and are important for campaigns aimed at better informing the public about the risk of UV radiation. Moreover, it is noteworthy that in the SU.VI.MAX study, use of sunbeds was more frequent among the youngest generations, it being recalled that the minimum age for inclusion in this cohort was 35 years for women and 45 years for men. Childhood is the period of life when intense exposure may have a substantial impact on the subsequent risk of cancer, but the only study available on this aspect is limited to a single French region and dates from 1993. Measuring such exposure is also a way of monitoring the real impact of preventive education campaigns on this topic, in order to make adjustments in the messages and actions of these campaigns.

Individual dosimeters can be used for direct measurement of the UV dose received by the skin, supplementing the data collected through self-administered questionnaires. There are several types of such dosimeters: polysulfone film badges that react to a broad UV spectrum but have the disadvantage of being quickly saturated; films containing *B. subtilis* spores, which are sensitive to erythemal UV radiation (Moehrle et al., 2000; Moehrle et al., 2000); and individual digital dosimeters worn on the wrist (Thieden et al., 2000) that measure only UVB radiation or a UV band fitted to the erythemal curve. Digital dosimeters that can record UVA and UVB exposure over long periods have been developed (Autier et al., 2000) and used to measure the exposure of children and adults during ordinary life or on holiday (Thieden et al., 2004; Autier et al., 2000; Rigel et al., 2003) and the exposure of professional athletes (Moehrle, 2001; Moehrle et al., 2003). A recent study measured exposure to erythemal UV radiation among preschool

children, during outdoor activities at nursery school, and compared the data from the biological dosimeters worn on the children's shoulders with the ambient UV measurements obtained using the same dosimeters placed in fixed locations on the roof of the school and with measurements of total ambient UV radiation provided by the Swedish Meteorological Institute (Boldeman et al., 2004). Quite recently, a study by the EORTC's Melanoma group showed that measurements of UVA and UVB exposure taken with electronic dosimeters correlated well with UVA and UVB irradiation data from a weather satellite (Boniol et al., 2005). Although the EORTC studies included French subjects, no study to date has measured the long-term exposure of French population segments to natural UV radiation. The use of meteorological data, supplemented by a detailed description of outdoor activities and of the environment (full sunlight or shade), should make it possible to evaluate the UV doses received by substantial segments of the population.

III.1.5 UV exposure and occupation

There is little documentation on work-related exposure to UV radiation. An evaluation of such exposure by occupation was made as part of an epidemiological study on ocular melanoma (Guenel et al., 2001). This evaluation, though rudimentary, gives a relatively complete picture of UV exposure in work environments. In the absence of usable data from measurements, UV exposure was evaluated on the basis of the judgement of industrial health experts. This evaluation involved determining indices of probability, frequency and intensity of UV exposure for each occupation defined by the five-digit International Standard Classification of Occupations (ISCO) code. In addition, solar UV radiation was distinguished from artificial UV radiation. A brief summary of the main findings of this evaluation is provided here.

Exposure to natural UV radiation (outdoor occupations)

Outdoor occupations involve exposure to solar UV radiation. The intensity and frequency of such exposure vary greatly from one occupation to another. They may also differ substantially between individuals having the same occupation, depending on local circumstances or the individual's activities. The main occupations exposed to solar UV radiation are listed in Table III-5. Seamen, fishermen and mountain guides are particularly exposed occupational categories (Moehrle, 2001; Moehrle et al., 2003; Moehrle et al., 1999; Moehrle et al., 2000).

Table III-5: Examples of occupations exposed to solar UV radiation

ISCO code	Designation	Intensity of exposure	Frequency of exposure
6.41-9.81	Seamen and fishermen	high	high
9.71	Dockers	high	high
6.22-6.23	Farmers and farm workers	average	high
6.31	Forest workers	average	high
9.73-9.74	Construction equipment drivers	average	high
9.51-9.52-9.53	Masons, construction workers, roofers, carpenters	average	high

7.11-7.12	Quarry workers, stonecutters	average	high
9.31	Building painters	average	average
8.57	Electrical and telephone linemen	average	average
1.80	Athletes and sportsmen	average	average
3.70-4.52	Postmen, street vendors	average	low
0.41	Aircraft pilots and navigators	low	low

Exposure to artificial UV radiation

Some occupations can involve exposure to artificially produced UV radiation. The main examples are listed in Table III-6. The spectrum of artificial UV radiation can be substantially different from that of solar UV radiation. In particular, it can include UVC radiation (arc welding), which is particularly harmful.

Table III-6: Examples of occupations exposed to artificial UV radiation

ISCO code	Designation	Intensity of exposure	Frequency of exposure
8.72	Welders (inc. arc welders)	high	high
8.73	Sheet-metal workers, boilermakers	high	average
8.93	Metallurgical furnace operators	average	high
8.71	Plumbers	average	average
8.74	Structural steel workers	average	average
8.91	Glass blowers	average	average
5.70	Beauticians	average	low
7.24	Metal casters	low	average

Associated risks

- Risk to the skin

A number of studies show a negative association between exposure while engaged in an outdoor occupation and the risk of melanoma (Elwood et al., 1997), suggesting that people who work outdoors have a lower risk of melanoma than those who work indoors. However, work-related exposure is associated with increased risk of epidermoid carcinomas and basal-cell carcinomas (Herity et al., 1989; Morales Suarez-Varela et al., 1992).

- Other risks

- Non-cancer risk:

Exposure to UV radiation emitted by arc welding causes ocular burns, well known to welders under the name of “arc flash”. A risk of cataracts has been described among oyster farm workers on the Chesapeake Bay (Delaware, USA) (Javitt et al., 1994; Taylor, 1989).

- Cancer risk:

Exposure to artificial UV radiation has been linked to an increased risk of ocular (choroidal) melanoma. The risk factors identified point to two types of activities that are probably mutually exclusive (use of sunbeds and pursuit of certain occupations, particularly arc welding). The association between ocular melanoma and the use of sunbeds has been shown by case-control studies (Holly et al., 1990; Tucker et al., 1985; Vajdic et al., 2004). Arc welding (which generates large amounts of UV radiation) is associated with greatly increased risk of ocular melanoma; in France, a study estimated this risk at 7.3 (95 per cent CI: 2.6-20.1) (Guenel et al., 2001; Holly et al., 1990; Tucker et al., 1985).

IV Cosmetic products and UV radiation[6]

IV.1 Sun protection products

IV.1.1 Types of sunscreens and how they work

Properties expected of a cosmetic sun protection product

Given the properties expected in terms of protecting the skin against UV radiation (UV absorption, skin biology), a sun protection product must satisfy the following specific requirements: sun protection, safety, local tolerance, stability and resistance to water and perspiration. In addition, as a cosmetic product it must be pleasing to the senses.

Regulations and assessment of UV screens

Appendix VII of the 26th European Commission Directive 2002/34/EC adapting Directive 76/768/EEC for technical progress lists 27 sunscreens that may be contained in sun protection products and sets the maximum concentrations allowed and the conditions of use for each. Some of the 27 sunscreens listed in Appendix VII of Directive 2002/34 are rarely used. Examination of the list of sunscreens most often found in products currently on the market, drawn up by manufacturers, shows that virtually none of them covers long wavelength UVA radiation. Internationally, the regulatory frameworks of Europe, Japan and the United States show some differences as regards the type and number of sunscreens permitted (the US Food and Drug Administration has a list of 16 sunscreens), the maximum concentrations permitted and the status of the products that contain them (over-the-counter sale in the United States).
Before UV screens are put on the market, they are evaluated for safety and efficacy. In Europe, this evaluation is conducted by the Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP; in 2004, it became the Scientific Committee on Consumer Products, or SCCP) in accordance with the SCCNFP guidelines ("Notes of guidance for testing of cosmetic ingredients for their safety evaluation"), the 5th revision of which was adopted on 20 October 2003. There is no specific evaluation of the UV protection agents in sunscreens. Apart from tests for phototoxicity and photosensitivity, the evaluation process is the same as that for the other ingredients, taking into consideration their specific properties, concentrations and area of application.
The evaluation is based on knowledge of the toxicity of the ingredients. The UV absorbency of the finished product is affected by biological and technical factors, as variations in these factors can change what becomes of the substance once applied to the skin.

Evaluation of the effectiveness of sun protection products

Sun protection products must be effective and hence must be proven to maintain their photoprotective power under reasonably foreseeable conditions of use. The stability of

[6] This section is drawn mainly from the work of the Afssaps expert group.

the finished product must be assured. This evaluation is based in particular on measurement of UV protection indices.
Evaluation of effectiveness involves, among other things, **measurement of protection indices**. The protection coefficient determined in this way is called "**static**", since it provides information on photoprotection at a given moment but not on how long it remains active, as certain factors are often not taken into account, such as perspiration, rubbing that removes the product from the skin, contact with water, the penetration of the product over a longer period, and the physical activities of users. The evaluation must also consider the "persistence" of sunscreens, i.e. whether they remain effective under normal conditions of use for a sufficiently long period.
The evaluation of the finished product also includes specific trials and topical bio-availability studies in order to assess the "**dynamic**" aspect, including a number of factors that may modify the effectiveness of the sun protection product:

- the substantivity of the product, as sunscreens that are easily removed from their target site offer less long-lasting protection;
- the time elapsed between application of the product and exposure to the sun, i.e. the latency period required for the product to act;
- time required for application;
- persistence of the product.

The substantivity of sun protection products, which is amply described in the literature, is connected in particular with their ability to adhere to or combine with keratinized substrates. Some sun protection products may form a surface film, others diffuse into the skin and attach themselves to keratinized substrates. The sunscreens belonging to the former category are easily removed from their target site and their protective power will not last long, whereas the latter will be highly persistent.
The physical parameters that affect adsorption are the same as those that influence skin penetration, namely: the concentration, molecular size and molecular configuration of the applied substance, the pH and hydration of the horny layer, possible interactions between the adsorbed product and the "fibrous proteins-lipids-water" complex of the horny layer.
The set of methods used serves to evaluate the product's effectiveness and ensure that it is safe. Each method is used to measure and evaluate one or more parameters, but none of them captures all of the parameters needed to determine a minimum duration of protection, especially since many of them cannot be controlled. This refers in particular to:

- the fact that displaying an application frequency defined in a solar simulator cannot capture all the geographical factors that determine the amount of sunshine (longitude, latitude, etc.);
- the fact that displaying an application frequency defined in terms of water resistance in standardized conditions cannot capture all the possibilities regarding how many times and how long the user goes in the water;
- the fact that displaying an application frequency defined by local bio-availability studies cannot capture real-life conditions related to imperceptible perspiration, the rate at which sweat is produced and evaporated, and hence to the frequency of re-application;

- the fact that displaying an application frequency defined in standardized conditions cannot capture the extent of users' physical activity (most sun protection products are subject to a sharp fall in their protection indices after 30 minutes of physical exercise).
-

IV.1.2 Sunscreen effectiveness

The methods used to assess sun protection, both *in vitro* and *in vivo*, help to demonstrate that external UV protection agents are effective in preventing solar erythema (sunburn).
Where the long-term effects of UV radiation are concerned, there is no scientific proof of a correlation between the use of sun protection products and protection against a biological effect, since the action of a UV protection agent on a biological effect can be measured only indirectly.
Current scientific knowledge on the subject is summarized in Table IV-1 below.

Table IV-1: Current state of scientific knowledge on the effectiveness of sunscreens

Effectiveness of sun protection agents	Current knowledge	Limitations
Short-term effects of UV radiation		
Prevention of erythema	Real and documented	For dermatologists, prevention of erythema is not a meaningful parameter for ensuring protection against the cellular effects of UV radiation.
Long-term effects of UV radiation		
Prevention of skin aging	Human research studies on prevention of skin elastosis: in progress.	No proof in human studies of the effect of external sun protection agents in preventing skin aging; certain agents show promise in *in vitro* studies.
Prevention of photo-immunosuppression (PIS)	Studies in progress	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.
Prevention of skin	- Two Australian clinical studies show a decline in	No proof in human studies,

cancer	pre-cancerous keratosis after application of sunscreens. - Most of the arguments in favour of the protective role of sun protection products with respect to the appearance of skin cancers are based on studies performed on *in vitro* models. - A few animal studies have shown that sunscreens have beneficial effects on the promotion of light-induced tumours, but these studies are few in number, conducted under conditions that are not readily comparable and for the moment do not allow much to be predicted about effects on human beings. - Older studies on mice showed that locally-applied sun protection agents with sunscreens helped to delay the occurrence of non-melanoma skin cancers after repeated irradiation with UV sources emitting mainly UVB radiation. - These results have been contradicted in humans by some 15 epidemiological studies, all of which found a higher relative risk of melanoma or non-melanoma skin cancer among habitual users of externally-applied sun protection agents than among non-users. The difficulty lies in how to interpret these findings. Do they reflect a real effect of the sunscreens (incomplete protection, overly narrow spectrum, improper use) or a perverse effect due to an increase in users' exposure time after application of sun protection products?	except a single study on prevention of squamous-cell cancers and actinic keratosis (epidemiological studies of broad-spectrum products).

Effectiveness of sun protection products in prevention of solar erythema

Although sun protection products offer real, documented effectiveness in preventing sunburn, in practice this protection is not complete, owing to poor choice of protection index with respect to the solar UV index, insufficient repetition of sunscreen application, irregular spreading of the product and the fact that certain skin areas are forgotten.

Effectiveness of sun protection products in prevention of 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 fibres in cases of chronic exposure (Takeuchi et al., 1998).

Effectiveness of sun protection products against UV-induced immunosuppression

The aim of protection against photoimmunosuppression (PIS) should be to reduce light-induced skin tolerance and the promotion of skin cancer (Meunier et al., 1998).
This theoretical objective runs into a major difficulty, however, in that the product must not interfere with the physiological processes resulting from the interaction of skin and

sun, and must not disturb the equilibrium of immune reactions, an equilibrium designed to suppress any auto-immune skin reactions at all times.
Protection against PIS should therefore be transitory and suitable for high-risk situations. It may be provided through various means, notably the use of sun protection products.
Epidermal Langerhans cells and dermal dendritic cells play a key role in these photoimmunological processes, and the main objective of protection against PIS is to preserve and maintain the "sentinel" function of these antigen-presenting cells (Meunier, 1999).
In most cases, for both mice and humans, the application of sunscreens helps to prevent a light-induced decrease in the number of epidermal Langerhans cells. Sunscreens also seem to protect Langerhans cells against UV-induced functional alterations. When applied to human tissue explants, they offer complete protection against decreases in the antigen-presenting capacity of epidermal cells from irradiated skin.
In humans, the application of a sunscreen before exposure to a strong UVB dose prevents CD36+DR+CD1a- macrophage cells from infiltrating the epidermis and prevents the modifications in T lymphocyte proliferation observed after a mixed epidermal cell-lymphocyte reaction (Meunier et al., 1995).
Protection indices, however, are not correlated with the capacity to preserve skin immunity. In humans, for instance, a chemical sunscreen (SPF 12) or a mineral screen containing zinc oxide (SPF 16) offer complete protection against erythema 24 hours after a UVB dose equal to four MED units. These sunscreens also prevent UVB-induced IL-10 transcription, but reduce only in part the migration of epidermal Langerhans cells (Hochberg and Enk, 1999).
In healthy volunteers, a single dose of UVA-I (340-400 nm) radiation equivalent to that received in a few hours of sun on a beach in summertime (60 J/cm^2) reduces the number of epidermal Langerhans cells and the antigen-presenting capacity of epidermal cells. Prior application of a sunscreen with a UVA protection index of 3 prevents only a part (60 per cent) of these functional alterations. This data points up the need to increase protection against long-wave UVA radiation by including sunscreens primarily intended to absorb this spectrum in product formulations (Dumay et al., 2001).
Although most studies have shown that sunscreens have a protective effect against the decrease in contact hypersensitivity reactions, the strength of this effect is highly variable. Some publications report complete protection, while others suggest that the coefficient of PIS protection is less than that of the inflammation. Moreover, a sunscreen having a high UVA protection index offers better protection against the decrease in contact hypersensitivity reactions induced by a solar simulator.
In *in vivo* studies on mice, the suppression of reactions to *Candida albicans* has been found to be caused by not only UVB but also UVA-II radiation (320-340 nm). The latter segment of the spectrum is held to play a vital role, since it induces a reduction of immunity equivalent to that of sunlight (Ulrich and Kripke, 2002).
In humans, chronic irradiation by solar simulator leads to a decline in delayed hypersensitivity reactions. This decline can be prevented by applying, before each exposure, a broad-spectrum sunscreen formulation with a UVB protection index of 30 and a UVA index of 12. Contact hypersensitivity reactions to nickel have also been studied after exposure of volunteers in a solar simulator. Here again, the decrease in immune responses can be prevented only by application of a sunscreen that stops both UVB and UVA radiation (Damian et al., 1997).

A study of 160 healthy volunteers sought to evaluate the protective action of a sunscreen formulation against cutaneous immunosuppression induced by UV radiation from a solar simulator. The model used involved induction of contact hypersensitivity reactions to dinitrochlorobenzene. It was shown that acute UV exposure, equivalent to intense sunburn, caused a sharp reduction in immunization against dinitrochlorobenzene and that prior application of a sunscreen having a UVB protection index of 15 and a UVA protection index of 9 offered effective protection against this drop in immunity (Serre et al., 1997).
In humans, a sunscreen formulation with a UVB protection index of 25 and a UVA protection coefficient of 14 prevents the decrease in contact hypersensitivity reactions induced by exposure to a solar simulator. These findings suggest that the use of sunscreens that protect against both UVB and UVA radiation helps to prevent a photo-induced decline in contact hypersensitivity reactions and delayed hypersensitivity reactions (Moyal and Fourtanier, 2001).
The current data concerning the ability of sunscreens to protect against PIS is reassuring on the whole. Sunscreens with high UVB and, most important, UVA indices provide effective protection against the decline in cell-mediated immune responses observed *in vivo* after UV exposure. Some human studies have pointed to the need for increased protection in the long UVA band for better prevention of UV-induced immunosuppression.
Prevention of immunosuppression effects requires the use of substances that limit DNA lesions, increase DNA repair capability (repair enzymes) and inhibit the release and activity of immunosuppressive cytokines. Knowledge of the mechanisms linking effects on DNA to immunosuppressive action should make it possible to develop new UV protection strategies (Meunier et al., 1998).

Effectiveness of sun protection products against photodermatitis

In reducing the quantity of UV radiation received by the skin, the use of sun protection agents forms part of the preventive treatment of all forms of photodermatitis. The effectiveness of sun protection agents in cases of polymorphous light eruption, which has been proven by some clinical research studies, is often only partial, reflecting incomplete coverage of the action spectrum of the photodermatitis concerned by the absorption spectrum of the photoprotection agent.
For these pathologies, which are often highly disabling, French dermatologists have called for high-index sunscreens (for both UVA and UVB) having a status allowing reimbursement of the patient by the public health insurance system.

Effectiveness of sun protection products against photo-induced carcinomas

Older research studies have shown that the application of topical sun protection agents of the sunscreen type delayed the occurrence of non-melanoma skin cancers in mice after repeated irradiation with UV sources that primarily emit UVB radiation. These results have been contradicted in humans by some 15 epidemiological studies, all of which found the relative risk of melanoma or non-melanoma skin cancers to be higher among habitual users of sun protection agents than among non-users (Huncharek and Kupelnick, 2002).

- In order for a sun protection product to be able to prevent carcinogenesis, the first requirement seems to be that its UVB and UVA protection coefficients be not too distant from each other.

The most rational explanation for this disturbing finding is guilty neglect of the role of UVA radiation: it is now clear that all types of UV radiation contribute to skin damage caused by the sun, through direct action affecting certain chromophores (UVB) and also through indirect mechanisms involving the generation of oxygen-reactive species (UVA and UVB).

In addition, spectral effectiveness depends on the biological effect considered. In fact, given the relative amounts of UVB and UVA radiation received during one day, it is accepted that in natural exposure conditions UVA radiation bears only 10 to 15 per cent of the responsibility for erythema, but perhaps 35 to 40 per cent of the responsibility for inducing cutaneous carcinomas. No publications in the current literature indicate the relative contributions of UVA and UVB to the various biological effects; the ratio cited above is based on a calculation in terms of the relative effectiveness of UVA and UVB radiation for the effect considered, based on experimental data. Where cancerogenesis is concerned, the calculation is based on De Gruijl's curve (De Laat et al., 1997) in comparison to the relative amounts of UVA and UVB radiation received during exposure to natural sunlight.

A topical sun protection agent with a high UVB protection coefficient and a "UVB protection coefficient/UVA protection coefficient" ratio less than 10 offers complete protection against sunburn. If, however, this ratio is greater than 1.5 or 2, the amount of UVA radiation not stopped by this topical sunscreen – an agent allowing prolonged exposure without erythema – 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 seems to induce people to prolong their exposure time. For example, Autier et al. (2000) have shown that while average daily exposure to the sun during summer holidays is 2.4 hours for users of an SPF 10 sun protection product, this figure rises to 3 hours for users of an SPF 30 sunscreen ($p < 0.05$). Such behaviour can increase the risk of skin cancer.
The development of new topical sunscreens offering better UVA coverage soon led to fresh research to dispel the worrying impression left by the epidemiological studies. Given the time it takes for cancers to form, these studies were mostly concerned with analyzing protection against two recognized factors in the generation of skin cancer, namely DNA damage and photoimmunosuppression, as well as against experimental cancerogenesis in mice.
For example, a sunscreen covering UVA radiation (especially the shortest UVA wavelengths) was assessed soon after its market launch for the protection it could offer against the formation of dimers (Ley and Fourtanier, 1997). Two sunscreens were tested in mice: a pure UVB sunscreen and a UVB-UVA sunscreen. After irradiation with a solar simulator (Schott WG 320 filter) delivering emissions similar to those of the sun at the seaside, both sunscreens offered significant protection against the formation of thymine dimers, with the UVB-UVA sunscreen performing somewhat better. After irradiation with a UVA-rich source (WG 345 filter), however, the UVB-UVA sunscreen was much more effective.

These results contradict those obtained in two studies on protection against photo-induced mutation of gene P53, in which it is observed that the addition of a UVA screen does not provide better protection than a pure UVB screen against P53 mutation, although the broader-spectrum sunscreen is more effective against P53 induction triggered by UV radiation (Berne et al., 1998; Seite et al., 2000).
In studies on mice using a solar simulator, the UVB-UVA sunscreen proved more effective than the UVB sunscreen in preventing UV-induced tumours (Fourtanier, 1996). Despite the clear superiority of the broad-spectrum sunscreen, it should be noted that low, repeated UV doses without photoprotection are less cancer-inducing than doses only twice as large administered after application of a sun protection product based on an SPF 4 UVB-UVA sunscreen. Protection against erythema is thus not correlated with protection against tumorogenesis, despite the extension of coverage to the UVA band. This study also found that increasing the concentration of the UVB-UVA sunscreen does not change its protective value against UV-induced tumours.
The most recent epidemiological studies, conducted with UVA-UVB protection agents, show that the latter can prove effective in preventing the appearance of new naevi (moles) in children (Gallagher et al., 2000), whereas an earlier study had shown that the use of sunscreens was correlated with an increase in the number of naevi (Autier et al., 1998). The latter result is important given that a link has been established between the number of naevi and the risk of melanoma[7].
A single study has shown that use of a broad-spectrum sunscreen can prevent the occurrence of squamous-cell carcinomas, but not that of basal-cell carcinomas (Green et al., 1999). This finding illustrates the complexity of cancerogenesis mechanisms, and hence the difficulty of preventing them.
In sum, the addition of UVA-blocking agents is probably a step towards enabling topical photoprotection to offer some protection against skin cancer.

- The second requirement is that one must not forget to apply the sun protection product regularly and in sufficient quantities.

The 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 evaluation of protection coefficients (2 mg/cm^2) (Bech-Thomsen and Wulf, 1992). This is important because the findings of

[7] Note by the Afsse expert group:

Nine published epidemiological studies have examined the relationship between the development of naevi in children and the use of sunscreens.

Six of these studies (Luther et al., 1996; Azizi et al., 2000; Darlington et al., 2002; Dulon et al., 2002; Wachsmuth et al., 2005; Bauer et al., 2005) confirm the positive association observed by Autier et al. (1998) between the number of naevi and the use of sunscreens, and none of them contradicts it. The most recent of these studies (Bauer et al., 2005), like that of Autier et al. (1998), finds the largest number of naevi among children who do not use sunscreen to protect themselves from the sun and shows that clothing offers excellent protection.

The study by Gallagher et al. (2000) is the only prospective interventional trial and remains the only study to have demonstrated a moderate reduction in the development of new naevi. However, the observed effect is concentrated in children with many freckles, and no effect was observed in children without freckles. The reason for this interaction with freckles is still obscure, but might be attributable to the fact that children with freckles are particularly sensitive to UV radiation. Very recently, a randomized prospective interventional study in 1,232 German children, monitored for three years, showed no reduction in the number of naevi associated with the use of sunscreens (Bauer et al., 2005).

Wulf et al. (1997) show a dramatic decrease in SPF when the quantity applied falls from 2 to 0.5 mg/cm^2.
Phillips et al. (2000) also emphasize the importance of observance. This study examines the protection offered against UV-induced histological damage after four consecutive days of irradiation, depending on whether the topical sunscreen is applied daily or intermittently (skipping one of the four days). It shows that regular use of an SPF 15 broad-spectrum sunscreen provides better protection than intermittent use of the same product and better protection than intermittent use of a narrower-spectrum product with an SPF twice as high.

- Conclusion

The role of sun protection products in preventing skin cancer is open to question owing to the fact that their effectiveness is not definitively established, that their coverage of the spectrum should be as complete as possible, that there is a need for careful use which does not however obviate all risk, such products require meticulous use, and finally to the cost of the products. As avoidance of the sun and wearing clothes as protection are not always easily compatible with certain leisure activities, broad-spectrum UVA and UVB topical photoprotection products may have a place in the prevention of skin cancer because they reduce the amount of UV radiation received by the skin.
Sun protection products therefore certainly do not constitute the basis of cancer prevention, and finding new strategies should remain a leading concern.

Effectiveness of sun protection products against melanoma

The relationship between melanomas, solar exposure and the use of sun protection products has been examined by many epidemiological studies. All of the studies have been analyzed, and their conclusions are summarized in the following paragraphs (Bastuji-Garin and Diepgen, 2002).

The findings of the case-control studies can be divided into four broad groups:

- Six studies are too biased to allow any conclusions to be drawn:
  - Two studies owing to a bias in selection of the control populations [Spain (Rodenas et al., 1996) and Austria (Wolf et al., 1998)].
  - Two studies without multivariate analysis [USA (Graham et al., 1985) and Norway (Klepp and Magnus, 1979)].
  - Two studies that take account of age, sex and phenotype, but not exposure to the sun [Denmark (Osterlind et al., 1988) and Sweden (Beitner et al., 1990)].

- Four studies with multivariate analysis show no link between the use of sun protection products and the occurrence of melanomas:
  - Two studies in which the sunscreen is a confounding factor [USA (Herzfeld et al., 1993) and Australia (Holman et al., 1986)]. The link identified disappears when phenotype and solar exposure are taken into account.

- Two studies in which the link between sunscreen use and melanoma disappears when age, sex, individual risk and solar exposure are taken into account [Italy (Naldi et al., 2000) and Australia (Youl et al., 2002)].

- Three studies show that sunscreen products have a protective effect. These studies take account of phenotype and solar exposure [USA (Holly et al., 1995), USA (Fisher et al., 1996) and Brazil (Bakos et al., 2002)]. In the study by Holly et al., however, exposure to the sun does not appear as a risk factor. The third study shows a protective effect even for sunscreens with a low protection index.

- Three studies with limited analytical biases show that topical sun protection products have a harmful effect. These studies take account of phenotype and solar exposure [Sweden (Westerdahl et al., 1995; Westerdahl et al., 2000) and Europe (Autier et al., 1995)]. However, questionnaire bias cannot be eliminated (particularly memorization bias), protopathic bias (reverse causality bias) cannot be eliminated, and the types of protective products used are not specified.

Other studies (Pincus et al., 1991; Azurdia et al., 1999) show that the recommendations for use of sun protection products are generally not observed (some areas of the body are often forgotten, not enough sunscreen is applied). Moreover, according to a study by Robinson, the average time elapsed between the beginning of exposure and application of sunscreen is 51 minutes.
As regards an association between application of a high-index sun protection product and increased solar exposure time, two randomized double-blind prospective studies conducted by the same research group among young adults show that the use of an SPF 30 sun cream was associated with an increase of approximately 25 per cent in exposure time (Autier et al., 1999; Autier et al., 2000) and an increase in UVB exposure (Autier et al., 2000). This result was not duplicated by another study conducted using a different methodology and an older population sample (average age 39 years) (Dupuy et al., 2005).
On the basis of all these studies, it emerges that no link has yet been established between the use of sunscreens and the occurrence of melanomas, in terms of both risk and protection (Huncharek and Kulpelnick, 2002; Dennis et al., 2003). The fact is that, given the contradictory findings of the studies, the lack of a dose-effect relationship and the lack of proof that exposure precedes the onset of melanoma, there are no grounds for associating the use of sunscreens with the occurrence of melanomas. Conversely, there is no proof that sunscreens provide protection.

Note (Afsse working group)
The effectiveness of sun protection products in preventing skin cancer and the non-carcinogenic effects of the sun is the subject of a monograph by the International Agency for Research on Cancer (IARC, 2001). The epidemiological and experimental data available in 2000 was analyzed in detail by an international working group, whose conclusions show no substantial difference from those of the Afssaps working group (see section II.2.4).

IV.1.3 Methods for evaluating cosmetic sun protection products

The methods used to evaluate cosmetic sun protection products are explained in detail in Appendix 1.

IV.2 Risks related to the association of UV radiation with cosmetic products other than sunscreens and dietary supplements (Afsse)

The pathologies classified under the general term "photosensitivity" constitute a huge set of conditions with different etiologies, all associated with abnormal skin reactions to radiation in the UV and visible spectra. These reactions may be caused by either sunlight or artificial light sources, and they present a great variety of clinical symptoms. Photosensitivity conditions may be divided roughly into two groups: genodermatitis and photosensitive reactions to certain chemical and pharmaceutical products. In addition, many pathological conditions may be exacerbated and in some cases triggered by UV radiation. We will discuss here only those photosensitive reactions that are linked to chemicals and molecules that may be used in cosmetic or pharmaceutical products.

Photosensitive reactions due to chemical products, either systemic or topical, represent a problem of growing importance, as new products are constantly arriving on the market. Once these agents penetrate the skin, they may absorb radiation and trigger an abnormal reaction. The reactions induced by UV radiation may be phototoxic, i.e. capable of affecting the entire population if the agent is provided in sufficient quantity, or linked to a biochemical and immunological reaction, which affects only part of the population. However, both types of reaction may be triggered simultaneously by the same molecule in the same individual.

The chemical mechanisms through which a substance is adsorbed and changes its structure under the effect of UV radiation are highly complex. Products of photoreactions, and possibly the oxygen-reactive species produced by the reaction as well, set off processes of cellular destruction (necrosis or apoptosis) that cause clinical signs to appear. The latter resemble severe sunburn, sometimes accompanied by blisters, and appear very soon after the irradiation, which may be of low intensity. The clinical signs vary considerably depending on the products involved, but generally this type of reaction is marked by the rapid appearance of erythema, accompanied by a burning sensation during exposure. The differences observed depend on the chemical reaction and on where in the epidermis the phototoxic product is located.

The drugs most often responsible for this type of effect are non-steroid anti-inflammatories, antibiotics, antifungal agents, diuretics, substances used to treat cardiovascular disorders, and behaviour modifiers. In this context, the behaviour of psoralens is unusual: irradiation stabilizes their interlayering between the DNA strands, thus adding photomutagenicity and photocarcinogenicity to the phototoxic effect. Most of these substances are activated by UVA radiation, although some reactions are more particularly dependent on UVB radiation.

A special case is the therapeutic use of the photoactivating and phototoxic properties of porphyrin derivatives to destroy tissue. These reactions are obtained through high-intensity visible light, which penetrates more deeply into tissue than UVA and UVB radiation.

A number of substances prove to be phototoxic when applied to the skin. They cause acute photodermatitis and rather frequently a photoallergic reaction with an eczematous rash on the areas exposed to sunlight. Here again, UVA radiation is the most frequent

cause of the reactions. The substances most frequently implicated include bergamot and citrus extracts (psoralens), polycyclic hydrocarbons (tars), perfumes (musk ambrette) and dyes (fluorescein). With the increasingly widespread use of sun protection products, phototoxic and photoallergic reactions to organic sunscreens have become more common, leading to the withdrawal of some benzophenones, para-aminobenzoic acid (PABA) and other substances.

It is not the task of the expert group commissioned by Afsse to provide complete lists of photosensitizing drugs and substances, since these lists will vary as certain substances are withdrawn and others arrive on the market. Annual analysis of the product descriptions colligated by the Vidal pharmacological dictionary might make it possible to compile a list, although any such list could not be exhaustive where either new or old drugs are concerned and would have to be updated continually, and although very little is known about the effects of drug combinations. Afssaps was recently assigned the task of drawing up a regularly updated list of photosensitizing drugs.

V European and international positions concerning UV-emitting appliances

V.1 Developments in the standardization of appliances designed specifically for tanning

V.1.1 Description of the IEC 60 335-2-27 standard

Appliances designed specifically for tanning were defined in an international standard prepared by the International Electrotechnical Commission (IEC). This standard came into effect in 1985. As its title indicates, it applies to all such appliances sold throughout the world, but it was not implemented in the United States, which follows the recommendations of the FDA (US FDA, "Sunlamp products, performance standards: final rule", 21 CFR 1040n Federal Register 50: 36548-36552, and US FDA, "Policy on maximum timer intervals and exposure schedule for sunlamps", Rockville, MD, 1986).
The IEC 60335-2-27 standard is part of the standard "Safety of household and similar electrical appliances: Part 2-27: Particular requirements for appliances for skin exposure to ultraviolet and infrared radiation". It was first printed in 1985 (IEC Technical Committee 61). At that time, a number of countries had introduced different technical standards concerning tanning devices.
The standard presents a classification of UV-emitting appliances that allows some national authorities to exclude certain types of appliances from their markets for reasons of health and user safety. The very title of the standard includes the word "safety", which applies not only to electrical and mechanical safety but also to the radiation emitted by the appliance. The standard underwent minor modifications in 1990 (2nd edition), 1995 (3rd edition) and 2002 (4th edition). Usually, once the international standard is approved by the European Standards/Electronic Standards Committee (CEN/CENELEC), it is implemented directly as a European standard (EN 60 335-2-27) and, in France, as a standard of the French standards agency AFNOR (NF-EN 60335-2-27). New editions of standards are published approximately every two years. The current (4th) edition of IEC 60335-2-27 was adopted in 2004. It should be noted that the French decree 97-617 dated 30 May 1997 is based on the **3rd edition published in 1995.**
According to the 3rd edition of standard 60335-2-27, UV-emitting appliances must belong to one of the types listed in the classification, the physical characteristics of which are presented in Table V-1.

Table V-1: Definition of types of UV-emitting appliances by effective irradiance

Types of UV appliances	Effective irradiance W/m²	
	250 nm < λ <320 nm	320 nm < λ < 400 nm
1	< 0.0005	≥ 0.15
2	0.0005 to 0.15	≥ 0.15
3	< 0.15	< 0.15
4	≥ 0.15	< 0.15

λ = radiation wavelength

The types of UV-emitting appliances are defined in Article 3 of the standard:

Type 1 appliance: appliance including a UV emission source such that the biological effect is caused by radiation of wavelength greater than 320 nm and characterized by relatively high irradiance in the 320-400 nm range.
Type 2 appliance: appliance including a UV emission source such that the biological effect is caused by radiation of wavelength less than or greater than 320 nm and characterized by relatively high irradiance in the 320-400 nm range.
Type 3 appliance: appliance including a UV emission source such that the biological effect is caused by radiation of wavelength less than or greater than 320 nm and characterized by limited irradiance over the entire UV radiation band.
Type 4 appliance: appliance including a UV emission source such that the biological effect is mainly caused by radiation of wavelength less than 320 nm.

Appendix 2 presents three examples of type 1 and type 3 tanning appliances found in tanning salons or sold to individuals. The left-hand column presents the emission spectrum as recorded by a spectroradiometer, and the right-hand column the erythemal effectiveness of these sources after weighting by the erythemal response of human skin. It can be seen that the erythemal risk of type 1 appliances stems primarily from UVA radiation, whereas the erythemal activity of type 3 appliances sold to the public is primarily concentrated in the UVB band. For the type 3 appliance TL 09, used both therapeutically and very often in solaria, the erythemal activity is divided equally between the UVB and UVA bands.

According to the standard, "The appliances must not be toxic or present a similar danger. Appliances including UV emission sources must not emit dangerous amounts of radiation and their effective irradiance must fall within the values specified in Table V-1."

Article 32.101 of standard 60 335-2-27 also specifies the conditions in which compliance checks should be conducted: aging of appliances before measurements and a distance of 0.3 metres.

V .1.2 Changes to the IEC 60335-2-27 standard

Document 60335-2-27 edition 2004-1, consolidated by amendment 1-2004, has been suspended pending the submission of an enquiry report by the European Commission, as the substantial changes included in it reveal major risks in terms of public health.
In 1990, Technical Committee 61 of the IEC, which is responsible for changes to the standard, decided to entrust the task of improving the standard to a group of delegated experts from a number of countries, in order to take account of technological advances and whether the tanning devices are safe. This experts group is now called Maintenance Team 16, or MT16. Despite the opposition of much of MT16 (which, it should be emphasized, is merely a consultative body), the secretariat of Technical Committee 61, which oversees publication of the standard as well as MT16, submitted for an international vote some substantial changes to the standard that might have serious

consequences in terms of public health if they were transposed into national standards and enacted as legislation in the countries having such standards.

In 2004, **amendment 1** (2004-07) to the 4th edition of the standard (2002-09) adds a type 5 UV appliance: an appliance including a UV emission source such that the biological effect is caused by radiation of wavelength less than or greater than 320 nm and characterized by relatively high irradiance over the entire UV radiation band. In addition, this amendment shifts the classification, which previously was normative in nature, to an appendix where it has merely informational status. Moreover, the maximum total effective irradiance is limited to 1 W/m^2 and the effective irradiance is weighted according to the action spectrum of skin cancer (International Commission on Illumination, or CIE). This limit (based on the skin cancer effectiveness spectrum) should be lowered to about 0.8 W/m^2 equivalent of the erythemal effectiveness spectrum. The whole of amendment 1 was drafted and submitted to international vote by the secretariat of the IEC's Technical Committee 61 without consulting MT16, which was opposed to it. The text was approved after a majority international vote. It should be emphasized that the majority of yes votes were made by countries that are **not concerned** by the safety problems of UV tanning devices, as these countries' populations consist mainly of Asian and African peoples, who are naturally protected against skin cancers (skin phototypes IV, V and VI).
The scientific experts of many countries consider that the upper limit of 1 W/m^2 (cancer) or 0.8 W/m^2 (erythema) is not acceptable, as this amounts, for 30 minutes of exposure (the usual maximum period of sunbed timers), to a dose of 1.28 kJ/m^{-2}, or 12.8 SED units. This corresponds to a UV index of 12, which is regarded as extremely high power (the tropical sun at noon), and four times the MED for an average skin phototype I or II. The risk of sunburn is therefore considerable.

In this new version of the standard, the definition of maximum radiation power is aimed at satisfying the European Commission, which had criticized the 2002 standard for not setting an upper limit for type 1, 2 and 4 tanning appliances. For this reason, the legislation in force in some countries prohibited, completely or partially, the marketing of type 1, 2 and 4 appliances (see section on this specific subject). It should be noted that type 3 appliances can be sold to the general public, as they are limited to 0.3 W/m^2 (erythemal), which for 30 minutes of exposure amounts to a dose of 0.48 kJ/m^2 = 4.8 SED = UV index 6, the equivalent of strong sunlight, which causes a light sunburn after 25 minutes of exposure for a pale-skinned subject.
Lastly, the latest proposal (**amendment 2**), currently up for international vote, would tend to abolish the current definitions of tanning appliance types and recognize only two classes: appliances for sale to the general public (the former type 3) and appliances for businesses providing UV radiation to the public. This proposal has not received the assent of the expert group. The French delegation voted no to all the proposals of amendments 1 and 2. In any event, it seems preferable that these changes in the international standard be transposed neither into European standards nor into French standards, the basis for French regulation.

V.2 International scientific positions

A number of international bodies have taken official positions **specifically** on the use of UV-emitting appliances for tanning. These positions are in almost all cases combined with recommendations on utilization for the safety of users. Virtually all of them discourage use of these appliances, and their recommendations for use are intended to ensure a measure of safety for those users who would disregard the advice not to use them. See also section II-2 for the analysis of risks by these bodies.

V.2.1 ICNIRP

The International Commission on Non-Ionizing Radiation Protection (ICNIRP) is an independent group of experts formed to evaluate scientific knowledge of the effects of non-ionizing radiation on human health. ICNIRP succeeded the International Non-Ionizing Radiation Committee (INIRC) of the International Radiation Protection Association (IRPA) in 1992. As a consultative international scientific body, ICNIRP is not concerned with the social, economic or political aspects of radiation protection. As its member experts are not affiliated with commercial or manufacturing businesses, ICNIRP is independent of all commercial interests. It is formally recognized by the World Health Organization (WHO), International Labour Organization (ILO) and European Union (EU) as a non-governmental organization working in the field of protection against non-ionizing radiation. It maintains close links with other scientific and technical organizations such as international standardization and research bodies. ICNIRP has published a statement entitled "General Approach to Protection against Non-Ionizing Radiation", spelling out its overall philosophy (ICNIRP Statement, 2002). It has also proposed exposure limits for both the general public and workers in terms of skin and eye exposure over an 8-hour period (ICNIRP Guidelines, 2004):

Exposure of the eyes. Ultraviolet radiant exposure in the spectral region 180 to 400 nm incident upon the unprotected eye(s) should not exceed 30 $J.m^{-2}$ effective spectrally weighted using the spectral weighting factors contained in Table I-2, and the total (unweighted) ultraviolet radiant exposure in the spectral region 315 to 400 nm should not exceed 10^4 $J.m^{-2}$.

Exposure of the skin. For the most sensitive, non-pathologic, skin phototypes (known as "melano-compromised"), ultraviolet radiant exposure in the spectral region 180 to 400 nm upon the unprotected skin should not exceed 30 $J.m^{-2}$ effective spectrally weighted using the spectral weighting factors contained in Table I-2. This limit should be considered a desirable goal for skin exposure to minimize the long-term risk, but it must be recognized that this limit is difficult to achieve in sunlight and judgment must be used in its practical application. It has a very substantial safety factor for dark skin phototypes (known as "melano-competent") and more generally for individuals who have been conditioned by previous, repeated exposures (known as "melano-adapted", i.e. tanned).

To determine the effective irradiance of a broadband source weighted against the peak of the spectral effectiveness curve (270 nm), the following weighting formula should be used: $E_{eff} = \Sigma E_\lambda . S(\lambda) . \Delta\lambda$,

where:

E_{eff} = effective irradiance in $\mu W.cm^{-2}$ or $W.m^{-2}$ normalized to a monochromatic source at 270 nm;
E_λ = spectral irradiance from measurements in $\mu W.cm^{-2}$ or $W.m^{-2}$;
$S(\lambda)$ = relative spectral effectiveness (unitless);
$\Delta\lambda$ = bandwidth in nanometers of the calculation or measurement intervals.

In its **Statement** on UV tanning appliances used for cosmetic purposes[8] after considering the effects of UV radiation on the skin and the various classes of UV tanning appliances, ICNIRP issued the following conclusions:

- [ICNIRP] recommends against the use of UV-emitting appliances for tanning or other non-medical purposes. People at particularly high risk should be particularly counselled against the use of tanning appliances:
    - People of skin phototype I or II;
    - Children (i.e. under 18 years of age);
    - People who have large numbers of naevi (moles);
    - Persons who tend to freckle;
    - Individuals who have a history of frequent child sunburn;
    - People who have pre-malignant or malignant skin lesions;
    - People who have sun-damaged skin;
    - Those who are wearing cosmetics, as these may enhance their sensitivity to UV exposure; and
    - Persons taking medication. In this case they should seek advice from their physician to determine whether the medication will make them UV-sensitive.

Should persons decide, in spite of the above recommendations, to use tanning devices, steps should be taken to minimize the risk (Appendix A to the ICNIRP Statement). After analysis of the effects on the skin and eyes and the risk of cancer and immunosuppression, the conclusions are clear and apply in particular to phototype I and II subjects and to children, as well as subjects displaying photosensitivity enhanced by the use of certain drugs or cosmetics or displaying a special risk owing to a pathology related to skin cancer.

V.2.2 WHO

In 2003, the World Health Organization published a document entitled "Artificial tanning sunbeds: risks and guidance"[9] as part of the Intersun programme, aimed at reducing the global risks connected with UV overexposure, which result from the socio-economic development of pale-skinned population groups in the industrialized countries and from the depletion of the stratospheric ozone layer. The document is available on the WHO website: http://www.who.int/UV/publications/sunbeds/en/. This document is based on the recommendations cited elsewhere herein – ICNIRP, EUROSKIN, NRPB and French regulations – and reproduces their most important points. The WHO document, which is addressed to political and socio-economic stakeholders in various

[8] ICNIRP Statement, "Health issues of ultraviolet tanning appliances used for cosmetic purposes", Health Physics 84: 119-127, 2003.

[9] WHO, "Artificial tanning sunbeds: risks and guidance", WHO, Geneva, 2003.

countries, particularly recommends that, before beginning a series of tanning sessions, customers be obliged to read the recommendations and sign a consent form, in order to ensure that they are fully aware of the risks.

V.2.3 EUROSKIN

EUROSKIN devoted a European conference with international participants to the problems raised by the use of tanning devices. A document published in the *European Journal of Cancer Prevention* in 2001[10] containing, in addition to a general statement on subjects who should not use tanning devices, a number of specific recommendations on the information that should be given to customers and the various provisions concerning how to operate the UV-emitting appliances. It should be noted that each of these recommendations reproduces an article of the French decree of May 1997.

V.2.4 NRPB

In 1995 and 2002, the UK's National Radiological Protection Board (NRPB) published a report entitled "Health effects from ultraviolet radiation", by a group of scientists specializing in public health[11]. Appendix B of this work is concerned in particular with the use of UV-emitting appliances and cosmetic tanning. This very complete document discourages the use of such appliances for tanning and recommends that users specifically, and the public in general, be informed of the risk of effects dangerous to human health. The document basically reproduces the positions of the American Academy of Dermatology (2001, 2004) and the Académie Française de Médecine (2003).

V.2.5 United States

An important step in recognition of the dangerous nature of artificial UV radiation was taken in 2002 under the US National Toxicology Program with the publication of the 10th edition of the report on carcinogens[12]. UVA, UVB and UVC radiation are all listed as agents reasonably assessed as carcinogenic for human beings. An entire section is devoted to exposure to the sun and to UV-emitting appliances. The report reminds readers that the American Medical Association presented a resolution in December 1994 requesting that the use of UV radiation for non-medical purposes be entirely prohibited. As the US regulatory system is based on the individual states, this report is of capital importance because it was prepared at federal level. Twenty-seven states have adopted regulations concerning the provision of artificial tanning sessions to the public.

V.3 Regulatory stances

[10] Greinert R., McKinlay A., Breitbart E., The European Society of Skin Cancer Prevention – EUROSKIN, "Towards the promotion and harmonization of skin cancer prevention in Europe. Recommendations", Eur J Cancer Prev 10: 157-62, 2001.

[11] NRPB, "Statement by the advisory group on non-ionizing radiation, use of sunbeds and cosmetic tanning". In: Health Effects from Ultraviolet Radiation 13, pp. 279-82, 2002.

[12] US Department of Health and Human Services, Public Health Service, National Toxicology Program, "The report on carcinogens", 10th ed., Dec. 2002.

V.3.1 List of official documents (regulations or health authorities' recommendations)

Table V-2: Legislation or health authorities' recommendations for selected countries

Austria	Presnorme Önorm S 1132 (01/01/2002), protective rules for operation of solaria where UV radiation is emitted.
Belgium	"Royal decision on requirements for exploiting solaria", 2000.
Canada	"Lignes directrices pour les propriétaires, les opérateurs et les usagers de salons de bronzage" (Guidelines for owners, operators and users of tanning salons) (Comité de radioprotection fédérale-provinciale-territoriale – Federal, provincial and local Radiological Protection Committees). Implementation of the regulations of the RED Act: regulations on sunlamps, 2002-03.
Finland	Decree on the limitation of public exposure to non-ionizing radiation (294/2002), section 4, Ultraviolet radiation. Supplemented by SS 9.1 (1989) on solarium safety and SONT 9.1 (2003) on solarium safety conditions and inspections (draft).
France	Decree 97-617 dated 30 May 1997 and implementing regulations dated 10 September 1997, 9 December 1997 and 16 September 2002 (see details below).
Germany	Certification of solaria (proposed by the Bundesamt für Strahlenschutz, Munich). Currently, UV exposure conditions in solarium must comply with Germany's DIN 5050-2: 06-1998 standard.
Netherlands	No formal legislation. Several reports (1987, 1994) from the Dutch Health Council.
Norway	Forkskrifter of 8 April 1983 on solaria/alpine sun. Delegation of authority: regulation by royal decree on the use of UV radiation for cosmetic purposes, 1 July 1983.
Spain	19574 Royal Decree 1002/2002 dated 27 September 2002: regulation on the sale and use of UV tanning devices.
Sweden	Regulatory code concerning sunbeds (SSI FS 1998: 2). Regulation of tanning devices used by the public complies with the criteria of the EN 60335-2-27 standard. 28 September 1998 and 3 November 1998.
USA	FDA Sunlamp Performance Standard 21CFR140.2, accompanied by a guide (1986) on timers and exposure frequencies.

We have no information for the following countries: United Kingdom, Switzerland, Italy, Portugal, Denmark, Poland and eastern European countries.

V.3.2 Comparison of the different legislations and health authorities' recommendations

To the best of our ability with the information at our disposal, we have tried in Appendix 3 to identify the most significant comparative features. The comparison yielded a few important points that may be mentioned here.

It was found that most of the Nordic countries have, for reasons of consumer safety, allowed only type 3 UV appliances to be used, setting the limit for both UVA and UVB radiation at 0.15 $W.m^{-2}$, i.e. a total UV irradiance of 0.3 $W.m^{-2}$. This is the equivalent of the tropical sun (UV index 12), which the WHO terms "extreme". Some Nordic countries reported that such appliances are also sold to the public.

A joint public health opinion issued by the radiological protection and health authorities of five Nordic countries (Sweden, Finland, Norway, Iceland and Denmark) in 2005 recommends, in keeping with the positions of international (WHO, ICNIRP, 2003),

European (EUROSKIN, 2000) and national bodies (the French Academy of Medicine, the French Dermatological Society, etc.), that increased safety precautions be taken in the use of UV-emitting tanning devices.
http://www.sst.dk/upload/forebyggelse/cff/sol_hudkraeft/nordic_sunbed_position.pdf

It should be noted that the main countries producing UV tubes and sunbeds (the Netherlands, Germany and Italy) have not adopted legislation placing limits on manufacturers. The United States has restrictive regulations imposed by the FDA, which has never recognized the IEC 60335-2-27 standard. An attempt has been made within MT16 to align the IEC standard with the FDA standard, primarily where safety objectives are concerned; obviously, this runs counter to the wishes of manufacturers, who want to market all types of UV appliances, even those that fall outside the current standards (type 5).
The European Commission has rightly expressed concern over the lack of power density upper limits for type 1 and 2 appliances (this does not concern type 4 appliances). Under pressure from manufacturers, an upper limit of 0.6 $W.m^{-2}$ eff (UV index 24), or 1 $W.m^{-2}$ NMSC, has been proposed. This limit seems particularly dangerous since all the appliances are equipped only with 30- or 60-minute mechanical timers, which, if the full timer duration is used, deliver erythemal quantities of radiation that are frankly unacceptable in terms of user safety. Timers are a central issue in the discussions with the FDA, which does not want to exceed a maximum possible dose of 4 MED (4 x 200 $J.m^{-2}$ eff).
Spain has legislation requiring that customers sign a register and an informed consent form and that they have a tanning log book indicating their schedule of tanning sessions, which should be suited to the characteristics of the UV appliance. This initiative has given rise to recommendations from the WHO (2003) and should be adopted in the French regulatory framework, which would allow better monitoring of the artificial UV radiation received by the population.
The total cumulative annual dose allowed, which is currently set at 15 $kJ.m^{-2}$ eff, stems from the 60335-2-27 standard. This is clearly a very large dose for the palest skin types (phototypes II and III), as it is considerably greater than that received through exposure to ambient natural UV radiation, which already causes a large number of skin cancers. Finland wishes to set a total annual dose no greater than 5 $kJ.m^{-2}$ eff. It has been demonstrated, moreover, that three sets of ten tanning sessions per year are practically enough to ensure a permanent tan, with the fourth “set” being natural exposure to the sun during the holidays. In these conditions, the maximum annual dose should depend on the phototype – 9 $kJ.m^{-2}$ (NMSC) for phototype II, 15 $kJ.m^{-2}$ (NMSC) for phototype III, 21 $kJ.m^{-2}$ (NMSC) for phototype IV – which is not clearly specified in standard 60335-2-27.

V.4 Current state of regulations and results of technical inspections in France since the regulations were implemented

V.4.1 The decree and its implementing regulations

Decree 97-617 dated 30 May 1997 relating to the sale and public availability of certain tanning devices that use ultraviolet radiation.
The decree consists of 20 articles and 3 appendices (on mandatory registration, content of instructions for use and informing the public). The decree is supplemented by three executive orders.

Order dated 10 September 1997 relating to the training of staff who use UV-emitting tanning devices made available to the public.

Order dated 9 December 1997 relating to the terms of certification of bodies authorized to inspect UV tanning devices.

Order dated 14 September 1998 listing the specialized bodies certified to carry out technical inspections of UV tanning devices. This list is updated regularly.

The important points of decree 97-617 may be summed up as follows:

- The classification of appliances follows that of the 1995 IEC 60335-2-27 standard. Only type 1 and 3 UV appliances are permitted.
- It excludes phototype I subjects and minors from using these appliances.
- It provides for specific training for operators, who must always be present when tanning sessions are in progress (automatic machines are excluded).
- It provides for mandatory declaration of UV appliances to the prefect (the DDCCRF or DDASS of the territorial department concerned) and an initial inspection of appliances, followed by inspections every two years, in accordance with a technical guide that certified inspection bodies are required to follow (see below).

V.4.2 Technical inspections

The circular of 16 September 2002, DGS SD7/DGCCRF no. 2002/486, defines the content of the technical guide for inspection of tanning installations, to be carried out by certified inspection bodies.

Specific points for technical inspections (some points in this guide are based on the content of the NF-EN 60335-2-27 standard):

Point 1:	Inspection of sunbeds (hygiene and mechanical safety)
Point 2:	Inspection of ceiling fixtures (high-pressure and low-pressure safety)
Point 3:	Inspection of high-pressure and low-pressure emitters, verification of appliance class
3.1	Inspection points: 25 cm from emitter and/or in contact with horizontal plate (bed)
3.2	Inspection procedures: five-minute pre-heat, verification of class, tolerance of plus or minus 30 per cent for UVB radiation, plus or minus 15 per cent for UVA
3.3	Measurement instrument: Solatel spectroradiometer (ambient temperature below 30°C)

Point 4: Electrical safety inspection (appliances and electrical installations), earthing, timer control, duration of operation
Point 5: Inspection of quality of attachments
Point 6: Inspection of ventilation systems
Point 7: Checking that goggles are supplied, verification of CE markings (directives 89/686/EEC)
Point 8: Checking the information provided for the public (Appendix 3 of decree), availability for users
Point 9: Checking of documentation (instructions for use of appliances)
9.1 Receipt acknowledging declaration to the Prefecture
9.2 Compliance with Appendix 2 of the decree
9.3 Previous technical inspection form (less than two years old), posting of inspection acceptance certificate
Point 10: Checking of staff qualifications: training certificate (less than five years old). Checking on updating of staff knowledge by certified occupational training.

V.4.3 Inspection results (details in Appendix 4)

Since 1999, a regular meeting of inspection bodies, representatives of appliance manufacturers, the Ministry of Health and the DGCCRF has been held to review the conduct and results of inspection operations and propose improvements. In 2004, the DGCCRF and the DDASS for each territorial department provided a review of their administrative checks. The group of physicians who train the instructors who will teach in cosmetology schools and vocational high schools also prepared an overview of its teacher training activities.

VI Conclusions

VI.1 Responses to the questions referred to Afsse

- **Works published or in press concerning the health effects of exposure to UV radiation and of the use of UV-emitting tanning installations**

A review of all the works published or in press concerning the health effects of exposure to UV radiation and the use of UV-emitting tanning installations yielded the following information:

Exposure to UV radiation has one beneficial effect on human health, but the dose of UVB radiation necessary and sufficient for vitamin D synthesis is well below 1 MED per week. Exposure to UV radiation also has harmful effects, in both the short and long terms, on the skin, eyes and immune system.

Exposure to UV radiation is carcinogenic for human beings. This effect has long been known for UVB radiation (280-315 nm), whereas the mutagenicity of UVA radiation has been demonstrated more recently.

The DNA lesions produced by UV irradiation depend on the wavelength of the radiation, and are caused by different molecular mechanisms. UVB radiation is a direct cause of pyridimine dimers and photoproducts, the repair of which can lead to the appearance of UVB signature mutations (C – T or CC – TT transitions). UVA radiation acts through oxidative mechanisms and can produce UVA signature mutations (T – G transversions).

Exposure to solar UV radiation is the main environmental cause of both non-melanoma skin cancer (epidermoid carcinoma and basal-cell cancer) and melanoma.

Prevention of skin cancer requires reduction of exposure to the sun. This recommendation should not be called into question on account of a recently published study indicating that patients show a higher rate of survival when melanoma is accompanied by histological lesions from solar elastosis, as this result may be due to the heterogeneity of melanomas.

Similarly, the results of recent epidemiological studies linking a reduction in the incidence of certain tumours (lymphomas) to solar exposure need to be confirmed and studied in greater depth (in one of these studies in particular, solar keratosis was still a risk factor). Moreover, no demonstrated mechanism can currently be put forward to explain these apparently beneficial effects of exposure to the sun, and there is no reason whatsoever to retract the European Code against Cancer recommendation to avoid excessive exposure to sunlight.

Concerning the use of artificial UV sources for tanning purposes, this practice was long considered to be risk-free and even able to provide protection against the harmful effects of natural irradiation. We know today that this is not true. In certain (melano-competent) individuals, exposure to UVA radiation induces a redistribution of pigment

without increasing melanin synthesis and without increasing the thickness of the horny layer of the epidermis. This short-lived "cosmetic" effect provides no protection whatsoever against the effects of UVB irradiation, and the UV doses received during artificial tanning sessions are added to those received during natural UV exposure, thus increasing the risks.

The risk of melanoma associated with tanning through exposure to artificial UV sources has been the subject of many epidemiological studies. The recent publication of a meta-analysis of nine studies and of a very large prospective cohort study allow us to assert today that tanning through exposure to artificial UV radiation increases the overall risk of melanoma by a factor of 1.25, i.e. an increase of one fourth. This risk is further increased by early or frequent exposure (by a factor of 1.6 to 1.7, and in the case of women who engaged in artificial UV tanning from 20 to 29 years of age the factor rises to 2.6, an increase of 160 per cent).

Where other skin cancers are concerned, fewer studies are available, but a recent publication suggests that the increase in the risk of epidermoid cancer and basal-cell cancer is roughly the same as the increase in the risk of melanoma (1.5 to 2.5).

It should be noted that a moderate increase in risk can bring a considerable increase in the total number of patients when a sizeable portion of the population is exposed. The increase in artificial UV tanning observed today is a source of concern in terms of public health.

- **The relevance of using limit values based on the minimum erythema dose to evaluate carcinogenic risks**

In the international IEC 60335-2-27 standard, the erythemal effectiveness spectrum of UV radiation in the 250-400 nm band is used to evaluate the erythemal risk of artificial UV sources and to define the various classes of UV appliances. This spectrum is also used to evaluate the dose delivered during the first irradiation session and the emission power of appliances. It should be recalled that this spectrum is an IEC/ISO standard (1997). The spectrum was derived from several previous erythemal effectiveness spectra obtained from study of human skin. The carcinogenic (non-melanoma skin cancer) effectiveness spectrum of UV radiation was standardized by the IEC in 2002. It is based on values resulting from carcinogenesis experiments conducted on hairless mice by research teams in Philadelphia (USA) and Utrecht (Netherlands). The tumorigenic effectiveness curve in mice (the SCUP-m curve) was adjusted to take account of the difference in UV absorption between human skin (which has a thickness of ~ 20 cellular layers) and mouse skin (~ 6 cellular layers). The tumorigenic effectiveness spectrum was introduced in amendment 1 to international standard 60335-2-27 in 2004 for calculation of the carcinogenic risk of UV appliances and of the recommended annual doses. Roughly speaking, it is multiplied by a factor of 2 for a given wavelength: for 325 nm UV radiation, for example, 0.6 W/m^2 on the erythemal spectrum corresponds to 1.0 W/m^2 on the tumorigenic effectiveness spectrum (for the nanometer-by-nanometer correspondences, see the weighting factors in Table I-2).

Experience has shown that the introduction of the carcinogenic effectiveness curve for non-melanoma skin cancers, which was done with the aim of reducing the total annual doses in accordance with this curve, has in fact caused confusion and may have contributed to the observed excesses. It would be preferable not to use this reference in the future in setting emission limits for the various types of UV appliances.

As the proportionality between the erythemal effectiveness spectrum and the carcinogenic effectiveness spectrum is fairly good, it does not seem necessary to introduce multiplication of the various action spectra. The erythemal effectiveness spectrum may thus be considered as representative of all effects.

- **The relevance of using lamps that emit only UVA radiation**

All suntanning is a response to an aggression by non-ionizing UVA and UVB radiation. Until 1990, as we lacked the technical capability to identify and quantify the DNA lesions induced by UVA radiation (lesions produced indirectly by oxygen-reactive species generated by absorption of UVA radiation by endogenous substances), it was thought that UVA radiation was safer than UVB when used for tanning purposes. The most recent studies, however, have demonstrated that UVA radiation induces mutations and cancer. In addition, it is mainly UVA radiation that causes photoaging.

From the standpoint of health, therefore, there is no point in using lamps that emit only UVA radiation in tanning devices.

- **Grounds for prohibiting the use of all cosmetic products during sessions in sunbeds, especially antioxidant substances**

There are a number of medical reasons for the prohibition of cosmetic products during tanning sessions:

- The application of water/oil or oil/water preparations on the horny layer and the epidermis induces increased penetration of UVA and UVB radiation.
- Topical preparations can convey photosensitizing, phototoxic or photoallergenic substances that cause abnormal reactions, increasing the genotoxicity of UV radiation.
- Any use of topical products containing photoprotective agents, such as UVB or UVA filters, changes the radiation received by basal-layer cells in an unpredictable and potentially dangerous manner.

As regards the use of antioxidant preparations or taking oral products intended to protect or restore the natural defensive capacity of the epidermis, the results obtained to date are too fragmented and incomplete to allow us to recommend such practices during exposure to natural or artificial UV radiation.

- **The most relevant European and international positions, both scientific and regulatory, on regulation of UV-emitting tanning devices**

The expert group adds its voice to the many warnings and negative judgements concerning tanning by artificial sources issued by a variety of national and international public health bodies (WHO, ICNIRP, EUROSKIN, NRPB, France's National Academy of Medicine) and unequivocally advises against the use of UV tanning devices. In addition, the expert group wishes to retain the classification of UV-emitting appliances used for tanning purposes as set forth in the NF-EN-60335-2-27 standard, 4th edition, 2000.

VI.2 Responses to the questions referred to InVS

- **Exposure of the population to UV radiation (InVS working group)**

Three complementary sources of data are currently available for measuring the natural (environmental) exposure of the French population to UV radiation.

The European SoDa programme, coordinated by the Paris School of Mines in Sofia-Antipolis (www.soda-is.com), measures solar radiation at ground level through observations made by weather satellites. Employing suitable algorithms, it estimates the proportions of UVA, UVB and erythemal UV in solar UV radiation. It has thus compiled a database constituting a time series of UV radiation data since 1985 (daily, monthly and annual observations) for France's entire territory, divided into squares 5 km to a side. The advantage of this system is that its grid completely covers France's national territory and that the measurements involved are easily taken. The database makes it possible to reconstruct the recent solar UV exposure of individuals or a given population. As it currently covers only 21 years, the archive cannot be used to calculate variations in UV exposure in relation to climate change.

Two ground-level stations in France are currently equipped with UV spectroradiometers, which are recalibrated regularly and have participated successfully in several European campaigns. These instruments record, at 30-minute intervals, the spectrum of total solar UV irradiance received at ground level in a horizontal plane. The Lille-Villeneuve d'Ascq station, located in a low-lying urban, industrial area and attached to the Lille University of Science and Technology (USTL), has been equipped since 1997 with a UV spectroradiometer with a Jobin Yvon double monochromator; it has been in regular use since 1999. The Briançon-Villard St Pancrace station, located in a moderately high mountainous area (1,310 m) at the Centre Européen Médical et Bioclimatique de Recherche et d'Enseignement Universitaire – CEMBREU (European Medical and Bioclimatic Centre for Research and University Instruction), which is run by Joseph Fourier University in Grenoble, has had two UV spectroradiometers in operation since 1999. One of these is similar to that of the Lille station, while the other uses a Bentham double monochromator with similar characteristics. These two stations for spectral measurement of solar UV radiation operate as a network. Their scientific purposes are as follows:

- to study the natural variability of this radiation and the various parameters that modulate it;
- to detect any long-term trends related, in particular, to human activity;

- to provide spectral UV data allowing validation of climatologies based on satellite observation;
- to make this data available to various communities of potential users (the medical community, biologists, photochemists, atmospheric chemists, etc.).

Lastly, from May to October, the French meteorological agency Météo France and the NGO Sécurité Solaire publish projections of the UV index (a general indicator of solar UV radiation) for metropolitan France. Initially, these projections were based on ground measurements taken by Sécurité Solaire at a small number of sites from 1994 to 1998 using broadband Robertson-Berger sensors, and on projections concerning the amount of sunshine and cloudiness. They are now generated by a chemical model of the atmosphere (MOCAGE) developed by Météo France. It remains to be demonstrated, however, whether the information derived from this system in any way converges with or complements the data from the other measurement systems described herein.

Considering the impact of intermittent exposure and the role of exposure in childhood, information on human behaviour with regard to UV radiation is very important in analysis of UV risk. Most of the information available today stems from studies of Western countries' populations (Australia, Canada, the United Kingdom, Scandinavia), which provide us with methodological principles and information for comparative purposes. The data on the French population is somewhat limited, but there are three studies available:

- The SU.VI.MAX cohort: A national cohort of volunteers participating in a controlled trial concerning absorption of dietary supplements. The cohort consists of 12,741 subjects, at least 35 years of age on their inclusion in the cohort, recruited in 1994 and monitored for 8 years. A nested analysis within the cohort provided information on the skin phototypes found in France and the subjects' behaviour with regard to UV exposure. This analysis showed that 22 per cent of women and 8 per cent of men reported that they had used artificial UV radiation.

- A 1993 cross-sectional study, based on a self-administered questionnaire, of 573 children aged 3 to 15 in the Montpellier area. The skin phototypes of this sample are described, and responses to the questionnaire are used to estimate total exposure to UV radiation over the summer.

- A national study, analyzed in 2001, was conducted during a randomized multicentre interventional trial for prevention and early diagnosis of skin cancer in health examination centres. The cohort consisted of a sample of 41,143 adults over 30 years of age residing in France and having had a periodic check-up in a health examination centre. This cohort provides information on adults' attitudes with regard to exposure to the sun, but was not intended to collect information on exposure itself, nor to determine the subjects' time budget with respect to UV exposure. In this study, 2 per cent of subjects reported that they use sunbeds. There is no obvious methodological explanation for the scale of the discrepancies in these results. The reason probably lies in the diversity of

behaviour with respect to UV radiation, particularly artificial UV radiation, but this aspect needs to be measured more accurately.

Lastly, individual dosimeters can be used for direct measurement of the UV dose received by the skin, in addition to the data from the questionnaires, and have been used to measure the exposure received by children or adults in ordinary daily activities or on holiday. A study by the EORTC's Melanoma Group showed that measurements of UVA and UVB exposure taken with electronic dosimeters correlated well with UVA and UVB irradiation data from the SoDa project. Although the EORTC studies included French subjects, no study to date has measured the long-term exposure of the French population to natural UV radiation. The use of meteorological data, supplemented by a description of outdoor activities and of the environment, should make it possible to evaluate the UV doses received by substantial segments of the population.

In conclusion, it is worth noting that to date there are no general studies of the French population, covering all age groups, on human behaviour with respect to natural or artificial UV radiation. The studies that have been conducted have served to validate the questionnaires and a methodology. The behaviour of teenagers and young adults, however, is entirely beyond the scope of these studies, despite the fact that these age groups are a commercial target for tanning businesses and are important to campaigns aimed at better informing the public about UV risk.

Work-related exposure to UV radiation is not well documented. In the absence of usable data from measurements, UV exposure was evaluated by determining indices of probability, frequency and intensity of UV exposure for each occupation defined in the International Standard Classification of Occupations (ISCO). In addition, solar UV radiation was distinguished from artificial UV radiation.

Outdoor occupations involve exposure to solar UV radiation. The intensity and frequency of such exposure vary greatly from one occupation to another. They may also differ substantially between individuals having the same occupation, depending on local circumstances or the individual's activities. Seamen, fishermen and mountain guides are particularly exposed occupational categories.

Some occupations can involve exposure to artificially produced UV radiation. The spectrum of artificial UV radiation can be substantially different from that of solar UV radiation. In particular, it can include UVC radiation (e.g. arc welding), which is particularly harmful.

VII Recommendations

VII.1 Exposure to the sun

Ultraviolet radiation plays a vital inductive role in the earth's ecological system and in the development of plants, animals and humans, yet exposure to solar UV radiation is also the primary cause of skin cancer and other health problems such as cataracts. The incidence of skin cancer is rising substantially in a great many countries, bringing death, suffering and disease at a heavy cost to health systems. The health authorities can, step by step, introduce measures to reduce the risks of exposure to both natural and artificial UV radiation to improve the health of the populations for which they are responsible.

The health authorities can make a significant contribution to controlling skin cancer:

- by creating a physical environment that offers shady areas, e.g. at bus stops, playgrounds, rest areas and schools;
- by encouraging photoprotective measures in schools and recreation centres;
- by inducing responsible behaviour on the part of businesses providing access to tanning devices or to natural solaria;
- by providing plentiful information liable to influence the public's knowledge, attitudes and behaviour through education and communication via the media.

Within the general population, children should be specifically targeted, as it is widely accepted today that children spend more time outdoors than adults and that they are more at risk of the carcinogenic effects of UV radiation. Strategies aimed specifically at protecting children should be encouraged in order to reduce the future incidence of skin cancer. The development of good habits in childhood helps substantially in ensuring regular use of suitable photoprotection in adulthood.

VII.1.1 A preventive approach

- **Increased use of the UV index**

Efforts to inform the public can be based on more widespread use of the UV index, a simple indicator of solar intensity. These projections, made by the national meteorological agency on the basis of measurements by ground and satellite networks, should be extended not only to areas offering tourist activities but also to summer resorts in the mountains, public swimming pools, amusement parks etc. The UV index would thus be associated by category with differing intensities of sunlight and with personal photoprotection items. Better knowledge of the UV index would certainly influence people's behaviour with respect to UV exposure and make it possible to reach them with simple messages on the prevention of skin cancer.

- **Preventing photo-induced skin cancers**

As excessive exposure to the sun plays a fundamental role in initiating and promoting skin cancer, so prevention necessarily involves reduced exposure to the sun and the use

of topical sun protection agents from the earliest childhood years, especially since the depletion of the ozone layer which threatens the third millennium will likely cause a dramatic rise in the frequency of skin cancers, particularly melanoma.

The aim is not to impose sweeping photoprotection measures on the entire population and throughout life, but rather to inform our fellow citizens about the dangers of UV radiation and to advise them as to ways of protecting themselves from it, particularly for individuals in the paler phototypes, people with many naevi and people exposed to intense sunlight.

The medical and paramedical professions are the best placed to deliver messages on primary prevention, many of which are simply commonsense advice:

- Teach people how to assess their own skin's sensitivity to sunlight.
- Remind them that the more sensitive their skin, the more gradual their exposure to the sun must be, and that they should avoid the hours when sunlight is most harmful, i.e. between noon and 4 p.m. in summertime (half of the daily UV dose is received during this four-hour period).
- Make clothing – a simple, inexpensive means of protection – the first line of defence by recommending that tightly-woven cotton clothing be worn.
- Recommend the use of topical photoprotection, with the aim not of increasing the number of hours of exposure but of protecting skin areas that cannot be protected by clothing, on condition that the sun protection product is effective against both UVB and UVA radiation. Products offering protection only against UVB should be prohibited, since, by suppressing the physiological warning represented by sunburn, they would allow overexposure to UVA radiation, which probably plays a much larger role in carcinogenesis than had been thought.
- Limit exposure to artificial UVA radiation and prohibit minors from using sunbeds.

The foremost target of primary preventive education should be parents, not only because they can control how much their children are exposed, but also because they can serve as an example for adolescents (who are exposed far too much) and give them advice. Photoprotective measures should begin in the earliest years of childhood, as the habits developed in childhood will then have every chance of persisting into adulthood.

- **Attract the attention of the resident population and tourists**

- Post signs to deliver messages about protection from the sun in densely-populated areas and areas where the risks of overexposure are high: stadiums, training grounds, public swimming pools, parks and gardens, the seaside etc.
- Distribute information leaflets about locations where the level of exposure to the sun can be high.
- Distribute information leaflets for parents with children in school.
- Distribute simplified leaflets to tourists.

- **Educational strategies**

- Educate people who run programmes and activities for young children, adolescents and adults.
- Inform supervisory staff in charge of outdoor activities.
- Encourage a multidisciplinary approach to sun protection, regardless of the educational level concerned.
- Encourage parents to follow the recommendations of the sun protection programme before children go to school or leave for outdoor activities.

VII.1.2 Proper use of sun protection

The expert group recommends effective use of sun protection items, but this term must not be taken to mean topical UV filters alone.

- Limit exposure during the hours when the sun is near its zenith (noon-4p.m.).
- Stay in the shade.
- Wear protective clothing suited to the temperature conditions.
- Wear a wide-brimmed hat to protect eyes, face and neck.
- Protect your eyes with wrap-around sunglasses offering UV filtration complying with the recommendations of the European Commission (types 1, 2 or 3). Type 4 sunglasses, recommended for intense sunlight, are not compatible with driving a car.
- Use topical sun protection products with a protection index of 15 or higher on areas not protected by clothing. It is recommended that such products be reapplied every two hours. One must be careful, however, not to let the use of sun protection products, particularly those with high protection indices, lead to an increase in exposure time. The reason for this is that the UVB protection index of such products is always much higher than the UVA index, and hence an increase in exposure time can increase the risk of skin cancer and skin photoaging. Campaigns should be conducted to inform the public of this.
- Keep children under one year of age out of the sun.

VII.2 Tanning facilities[13]

Analysis of the literature suggests that the UV radiation received in tanning sessions can constitute a substantial addition to natural UV radiation and thus contribute to the initiation of skin cancer. It is therefore recommended that people should not expose themselves to artificial UV sources. The health authorities have an important role to play in discouraging exposure to such sources, at least in the locations devoted to physical exercise that are under the authorities' control (swimming pools, gymnasia etc.).

There is no proof that the use of artificial tanning devices is less dangerous than exposure to the sun. Considering that exposure to UV radiation in general should be

[13] The National Academy of Medicine representative on the working group declared that he did not agree with the other members' conclusions concerning artificial tanning facilities, particularly as regards the regulation of such facilities. He expressed his views in a letter appended to this report as Appendix 6.

limited, the use of UV tanning devices for other than medical purposes cannot be recommended. People under 18 years of age and people who are particularly sensitive to UV radiation (skin phototypes I and II) are strongly advised not to use such appliances. Where they are used, it is necessary to limit annual UV doses and to provide users with all the information they need to reduce skin damage and all other health risks. In addition, it is important that tanning device operators be sufficiently well acquainted with the risks associated with UV radiation to help users reduce the risk to their persons and to avoid improper use of the appliances. Considering the importance of this personalized advice and of direct control, the use of automatic appliances is not acceptable under any circumstances.

The effective irradiance of a tanning device should not exceed the irradiance of the tropical sun, and the spectral distribution of its radiation should be fairly close to that of the tropical sun. The irradiance and spectral distribution should meet the specifications for type 3 UV appliances as defined in the EN 60335-2-27 standard (1997). The spectral characteristics (for both UVA and UVB radiation) and power levels of such appliances can vary widely. To facilitate the choice of a given appliance and inspection by the health authorities or national radiological protection authorities, the various types of UV appliances should be clearly identified, as should the sources of replacements.

In practical terms, the health authorities could:

- introduce or strengthen legislation in order to ensure that tanning device operators provide accurate and adequate information to their customers;
- conduct occasional inspections to ensure that eye protection is actually used;
- ensure that accurate information is given to consumers;
- put a stop to advertising claiming that the use of tanning devices carries no risk and may be good for one's health, and stop the promotion of artificial tanning;
- verify that proper hygiene is maintained;
- establish controls concerning the age limits at which customers can be admitted (over 18 years);
- provide specific guidance for adolescents on the dangers of artificial tanning (sun protection programme).

The expert group also echoes the positions of the WHO, which recommends that tanning devices not be used when the potential users:

- are of skin phototype I, i.e. they cannot tan and they burn easily;
- are under 18 years of age;
- have a large number of naevi (moles);
- tend to have freckles;
- have been subject to frequent sunburn in childhood;
- display pre-malignant or malignant skin lesions;
- have skin damaged by the sun;
- have applied cosmetics that might increase their sensitivity to UV radiation;
- are taking medication. In this case, the individual's physician is the only person qualified to determine whether the treatment makes the individual more sensitive to UV radiation.

VII.2.1 Limit values for exposure to artificial UV radiation

It should be recalled at the outset that the UV index of a type 3 tanning appliance is approximately 12, the equivalent of a tropical sun. If the proposed changes in IEC standard 60335-2-27 were implemented, they would allow a UV index of 24 – a level of exposure not reached naturally anywhere on earth.

Most medical and scientific bodies, learned societies and international organizations recommend avoiding exposure to artificial UV radiation. If some people choose to ignore these recommendations, however, it is advisable to set certain limits, while at the same time indicating that these limits do not make the use of UV appliances risk-free, particularly in cases where the person undergoes a large number of sessions:

- First exposure to UV appliances: 100 $J.m^{-2}$ E_{eff}
- Total annual exposure: three series of ten sessions for melano-competent subjects – phototype III, 15 $kJ.m^{-2}$ (NMSC); phototype IV, 21 $kJ.m^{-2}$ (NMSC)

Some clinical studies have shown that above ten annual sessions of exposure there is a significant risk of melanoma. The formula used to calculate risk predicted a significant risk of non-melanoma skin cancer.

VII.2.2 UVB/UVA ratio of tanning devices

The current regulatory framework in France (Article 8 of decree 97-617) provides that the irradiance in the UVB band (< 320 nm) of type 1 and type 3 appliances must not exceed 1.5 per cent of their total UVA + UVB irradiance. This provision could be eliminated for the sake of clarity and ease of interpretation, and replaced by a reference to the tropical sun at the zenith. The European Cosmetic Toiletry and Perfumery Association (COLIPA) and the European Commission have defined a standard solar irradiance, whose UVB/UVA ratio could be used as an upper limit value.

VII.2.3 Cosmetic products

Draft recommendations concerning the labelling of sun protection products are being developed at Afssaps

The first part of these draft recommendations covers the following items:

- The marketing of sun protection products offering both UVA and UVB protection.
- Harmonization of labelling to facilitate product comparison and choice by consumers.
- The wording and simplification of the technical information printed on the labelling to help consumers understand the risks.
- Classification of sun protection products in a limited number of categories according to defined criteria.
- Harmonization of the methods used to evaluate sun protection products.
- Information on proper use of sun protection products.

VII.2.4 Regulatory changes

It is recommended that the exposure time offered by sunbed timers be limited by indexing it to the total power emitted by the appliance, such that the latter cannot deliver more than 8 SED units.

- All melano-compromised subjects should be informed that under no circumstances should they be exposed to artificial UV radiation.
- The prohibition on minors should be strictly enforced.
- Following the recommendation of the WHO, the customer should be required to complete, sign and date an informed consent form before beginning any series of artificial tanning sessions. One copy of the form is for the customer, while the other must be preserved for two years by the tanning salon. This document, which must be presented at the request of inspection officers, as the latter are defined by the regulations, would provide more precise information on the use of tanning devices (Appendix 5 contains a proposed text for this consent form).
- The working group suggests that only type 3 appliances be allowed under French regulations; this will simplify inspections and avoid dangerous appliances that attempts to deregulate the industry would bring onto the market.
- Prohibition of advertising and promotion of tanning devices and of the establishments making them available to the public.
- Prohibition of all claims that exposure to artificial UV radiation offers health benefits.
- The power of UV tanning devices should be limited to that of a tropical sun (UV index 12, or 0.3 W/m^2 eff (weighted by the erythema action spectrum). This proposal would align the French position with that of the Scandinavian countries, where over 35 per cent of the population uses UV appliances but where people are much less exposed to the sun than in France.

VII.3 Other UV sources designed for domestic or industrial uses

At the request of the expert group, Afsse has formally requested the National Testing Laboratory (LNE) to take measurements in a variety of configurations in which "full-spectrum" lamps and tubes are employed for domestic or similar uses. Depending on the results obtained, it may be necessary to issue recommendations on the distribution and use of such lamps. The LNE has submitted the initial results from these measurements, which seem reassuring but cover only one type of lamp: Osram "Fluocompact" lamps, Dulux type, power 15 and 30 watts; and Osram tubes, Biolux L type, 36 watts/72-965. These emission sources are presented in some advertising materials as emitting a spectrum identical to that of the sun; in fact, this is not true, as they emit in a spectrum of discontinuous radiation. Moreover, despite the claims of distributors, the UV emissions of the Fluocompact bulbs and tubes are particularly weak, with appreciably less UVA than a traditional compact fluorescent lamp. In terms of UVB irradiance, the 15-watt lamp emits 0 UVB at all illumination levels (like a traditional lamp), while the 30-watt lamp and the 36-watt tube have UVB irradiance levels ranging from 0.2 10^{-9} W/m^2 to 4 10^{-9} W/ m^2 for levels of illumination ranging from 200 lux (reading) to 1,000 lux (workplace). The levels of UVA and UVB irradiance of these lamps, which are supposed to be representative of the solar spectrum,

are in fact practically the same as UV emissions from a traditional fluorescent lamp or tube. However, their UV irradiance is roughly 3 to 20 times less than that of a traditional tungsten halogen lamp, for identical levels of illumination. These lamps therefore cannot be considered to be significant sources of UV radiation, despite the claims of their distributors.

In the absence of data on the other types of lamps on the market, however, and particularly lamps initially designed for industrial use, we should give some consideration to recommendations that might be made.

These sources are designed to be used for direct illumination and to replace ordinary tubes and lamps, notably in the home and workplace. Among the risks to be considered are acute and long-term ophthalmic risks, photosensitization risks and risks of skin cancer. Limit values based on those used for exposure in work environments (ACGIH and ICNIRP) may be proposed. However, the UV irradiance depends on a variety of factors connected to how these lamps are used (number of lamps or tubes, distance to the lamp, direction etc.). As it would be futile to try to assess all configurations that might be met with, it is necessary to make certain assumptions, overstating the irradiance to a reasonable extent, in order to evaluate the exposure situations which users of such equipment may face. The main parameters used to determine the limits on use of these lamps are the distance to the source and the length of time they are used. Thus, 10 hours of exposure and a distance of 20 cm were selected as values to characterize the risks connected with use of "full-spectrum" lamps. On the basis of research by the ACGIJ and ICNIRP, the effective irradiance of the source at 20 cm (a plausible distance for desk lighting) should not exceed 0.8 mW/m^2. Moreover, in view of the fact that these limit values were established for well-informed workers, an additional safety factor should be introduced for the general public or uninformed workers in order to take the most photosensitive people into account.

The experts group would like to see the establishment of a regulatory framework (developed by the health and consumer affairs ministries) for any sources that exceed these limit values. These recommendations could be issued on the basis of the provisions of the Council Directive of 19 February 1973[14]. The regulations on the sale of and provision of public access to certain tanning devices that emit UV radiation could then be extended to all UV sources made available to the public. In selling full-spectrum lamps, manufacturers and distributors should therefore inform consumers on the risks of prolonged exposure to UV radiation and clearly explain the proper practices for use of their products. In fact, it seems that most of these products are not used for their initial purpose (e.g. horticulture). Statements that this type of lamp may have a beneficial effect on health or even that it can be used for ordinary day-to-day lighting should be prohibited. Their use in places of public assembly, particularly places where children are present, and as lighting for occupational premises should therefore be prohibited.

[14] The directive relates to electrical equipment designed for use within certain voltage limits and providing in particular for the adoption of technical measures such that radiation which could constitute a hazard is not produced.

VII.4 Proposal for UV exposure studies[15].

Recommendations for improving knowledge of the French population's exposure to UV radiation and improving knowledge of its effects on health

Improving knowledge of exposure

Recommendation 1: To improve knowledge of environmental exposure to UV radiation

As regards environmental exposure, two complementary systems exist, which must be supported and whose consistency should be encouraged.

SoDa project: www.soda-is.com

Measurement of exposure to UV radiation throughout the French territory has been conducted from a meteorological satellite, but only partly exploited. This project should be encouraged in order to create a database comprising a time series of UV radiation (daily, monthly and annual observations) for the whole country, by geographical cells measuring 5 km square. Exposure could be evaluated and monitored by associating it with a geographical information system.

Subsequently, these measurements could be associated with the available registers, and laws could thus be drawn up. By applying these laws to the whole country, a digital atlas of the distribution of exposure to UV radiation would be obtained. At the end of this study, an important source of reliable data for evaluation of the health impact of natural UV radiation would be obtained. It would also provide regional quantification of the risks affecting different categories of population. Conducting this study would require additional support for the SoDa programme, which is mainly funded by the Ecoles des Mines de Paris and Armines, the European Space Agency, the International Energy Agency and the ADEME. The study would be conducted in parallel with the work already planned, and would exploit its results. The work would be planned in such a way as to take account of the specific characteristics of this public health problem, including a quarter-hourly evaluation of UV radiation and increased precision of UV measurements.

Ground-level measuring stations:

The second system is based on ground-level spectral measurements. The sites of the two French stations are typical: one in an industrial zone without mountainous areas and with a high population density, and the other in an area where numerous tourists go in for snow and altitude sports. The influence of their particular atmospheric and orographic characteristics on UV radiation (ozone pollution, high aerosol content,

[15] This part of the recommendations was drafted by the InVS experts' group

altitude, relief and snow reflectance) could therefore be studied and monitored over the long term. A third station situated by the sea, and consequently in a typical place of our French coastal areas where large concentrations of summer visitors are exposed to UV radiation for long periods, would usefully complete the set of stations.

At the present time, the two existing stations are funded from the resources of the two laboratories that created and operate them: LOA in Lille, and the IRSA team in Grenoble. Unfortunately, there is no specific permanent funding to guarantee that they can continue to operate in future, as they are reliant on obtaining national or European contracts, which always have a fixed term.

The extension of the present network to three stations is certainly desirable and conceivable by involving a third laboratory in the operation of the new site. However, the size of the complex would require additional human resources to allow multi-annual data readings.

Satellite and ground-level measurements: a complementary approach.

These two systems are wholly complementary: the satellite system is based on measurements and calculation that provides complete coverage of the country, while ground-level measurements enable the model to be validated in several atmospheric situations. Coordination between these projects should be encouraged. The convergence and complementarity of these projects with the Météo France MOCAGE model should also be systematically studied as regards methodology, significance of indicators and feasibility.

Recommendation 2: To improve knowledge of behaviour relating to natural and artificial UV radiation

It is essential to evaluate practices relating to exposure to natural and artificial UV radiation by all age groups of the population, including children, teenagers and young adults. The studies conducted to date, both worldwide and on French populations, have provided a fairly sound methodology based on self-completed questionnaires. However, the French studies do not cover the whole population, and do not focus on the teenage and young adult age groups, which have the most leisure time and are the “commercial” target of tanning professionals. Intermittent exposure during holidays should also be evaluated, including for children.

If these surveys are repeated, the impact of prevention campaigns could be assessed on the basis of validated indicators (so that the messages of the campaigns can be adapted if necessary), and the interaction between exposure to natural and artificial UV radiation could be measured. These studies should be conducted in several regions of France to take account of the differences in distribution of phototypes, sunshine and behaviour in relation to natural and artificial UV radiation. These studies could be based on a self-completed questionnaire. The standard questionnaire would cover the characteristics of the respondents (age, phototype, sex and occupation) in accordance with an existing methodology [Rosso et al., 2002]. The questionnaire would be filled in by respondents every three months. It would relate to voluntary and involuntary sun exposure habits

(weekdays, weekend, winter and summer holidays) during the preceding three months. The questionnaire would include details of visits to swimming pools, fitness centres and establishments offering artificial UV treatment. The questionnaire could be completed by items giving information about the perception of the UV risk associated with immediate effects (sunburn, tanning, feeling of well-being) and long-term effects (photo-induced skin aging and skin cancer). In addition to answering this questionnaire, a smaller number of respondents could be directly examined in the context of school and occupational medicine by a dermatologist trained to recognise photoinduced skin lesions (solar lentigines and naevi) and phototypes. The number of respondents, which would necessarily be smaller, could be 1000 to 2000 and the direct examination being repeated every two years for six years. This examination could be completed by ultraviolet photographs allowing evaluation of early photo-induced damage in small children. The current technologies (UV sources and digital cameras) allow standardization and reproduction of documents [Pagnoni and Kligman, 1997]. Several cohort studies (adults and children) are currently being conducted to provide more information about environmental and nutritional exposure, and the addition of a "UV exposure knowledge" facet should be considered.

The practice of exposure to artificial UV radiation (tanning installations) should be specifically studied, by describing the financial data for this market (which have never been published), investigating practices, and endeavouring to better draw up more accurate profiles of the people who frequent these centres, the history of their exposure to UV radiation, and their motives. This could form the subject of a feasibility study.

Recommendation 3: To improve knowledge of advertising messages relating to exposure to UV radiation

This report does not analyze the social representations that support and encourage exposure to UV radiation of natural and artificial origin. These representations, which are strongly present in advertising messages, either directly or indirectly, are a major part of the reason for exposure to UV radiation. There are also open advertising practices aimed at the general public, the network of beauty treatment professionals, and health professionals. These messages probably represent the majority of the information messages regarding the UV risk received by the population, and are only moderately counterbalanced by health education messages. Knowledge of these advertising campaigns, analysis of their impact on the behaviour of populations, and conformity of the messages to legislation should be systematically pursued, as should work on knowledge of the social representations of UV exposure. This project could be included in the terms of reference of the National Health Prevention and Education Institute.

Recommendation 4: To improve knowledge of occupational exposure to UV radiation

Some jobs that are particularly exposed to solar or artificial UV radiation can present specific risks to health. This applies in particular to welders, who are at high risk of ocular melanoma, to maritime jobs and to mountain leisure jobs.

A better characterization of exposure to UV radiation in jobs exposed to artificial UV radiation seems necessary.

This characterization of exposure, conducted on a sample of exposed workers, could be useful, firstly for the conduct of epidemiological studies designed to confirm the links between UV radiation and risk of ocular melanoma, and secondly for the introduction of suitable preventive measures.

Recommendation 5: To coordinate actions in the field of knowledge of exposure to UV radiation; proposal for an observatory of human exposure to UV radiation

The actions required to improve knowledge of the population's exposure to UV radiation are based on a wide variety of skills. Their introduction and development should cover the different fields of UV exposure. This requires a global approach, a concerted strategy between the parties involved, and an operational structure. Such an approach could be coordinated by a body which could be called the "Human UV Radiation Exposure Observatory", and would be responsible for these actions and the production of indicators. Production of indicators would take account of European recommendations, in order to facilitate the comparability of the French data with those of other countries.

Such an observatory should employ metrologists familiar with the physics of UV radiation, skin cancer epidemiologists and dermatologists. It should guarantee the consistency of actions in the field and ensure that there are no population categories or practices which have not been studied from the standpoint of UV exposure risk. It is not necessary for this body to have an independent administrative structure: agreements between establishments could govern its operation, and InVS could handle its administrative requirements.

Recommendation 6: To improve knowledge of the effects of UV radiation

Non-melanoma skin cancers (squamous-cell and basal-cell carcinoma) are not subject to epidemiological surveillance in France. Knowledge of the incidence of these cancers does not necessarily require the creation of a register. In view of the moderate severity of these carcinomas, the complexity of the health care network that identifies them and their social consequences (e.g. an impossibility to take out loans), which suggest under-declaration, the methodology of these studies should be adapted and tested at a feasibility stage. Knowledge of the incidence of lesions indicating strong UV exposure, such as naevi, should also be obtained, primarily through feasibility studies [Autier et al., 1998; Daures et al., 1995]. However, population studies should be designed in such a way that they can be repeated, so that they constitute indicators of the history of past exposure at individual level.

VIII Abbreviations and acronyms

ACGIH: American Conference of Governmental Industrial Hygienists
Afssaps: Agence française de sécurité sanitaire des produits de santé (French Health Products Safety Agency**)**
Afsse: Agence française de sécurité sanitaire environnementale (French Environmental Health Safety Agency)
CIE: International Commission on Illumination (Commission Internationale de l'Eclairage)
COLIPA: The European Cosmetic Toiletry and Perfumery Association
CSHPF: Conseil supérieur d'hygiène publique de France (French Higher Public Health Council)
DDASS: Direction départementale des affaires sanitaires et sociales (Department of Health and Social Affairs at the level of French territorial departments)
DGCCRF: Direction générale de la concurrence, de la consommation et de la répression des fraudes (General Directorate for Competition, Consumer Affairs and Fraud Control)
EC: European Commission
EORTC: European Organization for Research on Treatment of Cancer
IARC: International Agency for Research on Cancer
ICNIRP: International Commission on Non-Ionizing Radiation Protection
IEC: International Electrotechnical Commission
InVS: Institut de veille sanitaire (Health Watch Institute)
MED: minimum erythema dose
MOCAGE: Modèle de chimie atmosphérique de grande échelle (Large-Scale Model of Atmospheric Chemistry)
NMSC: non-melanoma skin cancer
NRPB: National Radiological Protection Board
SED: standard erythema dose
SPF: sun protection factor
UNEP: United Nations Environment Programme
UV: ultraviolet
UVReff: effective UV radiation
WHO: World Health Organization
WMO: World Meteorological Organization

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X Members of the Afsse experts group

Jean-François Doré

Jean-François Doré is director of research at the French National Institute for Health and Medical Research (INSERM). He heads the "Cellular responses to genotoxics" team of INSERM Unit 590 ("Oncogenesis and tumour progression") at the Centre Léon Bérard in Lyon. He directs experimental research on the responses of human melanocytes to ultraviolet radiation, and coordinates international epidemiological studies on the role of UV exposure in the aetiology of melanomas and on measurement of the UV exposure of individuals and populations. He holds a doctorate in the human biology of experimental cancerology (1974). From 1964 to 1974, at the Institute for Oncology and Immunogenetics in Villejuif, he conducted research on the immunology of human leukaemia and melanoma. In Lyon, from 1974 to 1993 he directed the Immunology and Experimental Oncology Laboratory of the Centre for the Fight against Cancer, which during his term as director became INSERM Unit 218, and conducted research on the biology of invasion and metastasis. Since 1990, within the framework of the Melanoma Group of EORTC, of which he has been a member since its establishment in 1969, as well as serving twice as its secretary, he has developed international multicentre epidemiological studies. He is currently chairperson of the Epidemiology Committee. From 1994 to 2003, he was Honorary Senior Research Associate in the Epidemiology and Biostatistics Department of the European Oncology Institute in Milan. He has been a member of the Consumer Safety Commission (1987-93) and the European Commission's Scientific Committee on Cosmetics and Non-Food Products (1997-2000). He is a member of the Higher Meteorological Council. He received the Rosen Oncology Prize in 1969 and is a Knight of the National Order of Merit.

Jacques Bazex

Jacques Bazex took his degree as doctor of medicine in 1972. He is head of the Dermatology and Venereology Department at the regional hospital (CHR) in Toulouse (1984) and University Professor at the Paul Sabatier Toulouse III University (1988). He is a member of the French Society for Dermatology and Syphiligraphy, a member of the French-Language Dermatological Society, a member of the US Society for Investigative Dermatology, an honorary member of the Spanish Academy of Dermatology, a member of the American Academy of Dermatology, a member of the European Academy of Dermatology and Venereology and a member of the Society for Cutaneous Ultrastructural Research (SCUR). He has also been a corresponding member of the French National Academy of Medicine since 1997. His main research work has been on the physiopathology of leg ulcers, psoriasis, bullous diseases, neutrophilic dermatitis, paraneoplasic syndromes, follicular atrophodermia, systematic electron-microscope analysis of the main forms of dermatitis, and calcic deposits in scleroderma.

Jean-Pierre Césarini

Jean-Pierre Césarini is a doctor of medicine and holds a specialized studies certificate (CES) in pathological anatomy. Formerly a lecturer at the University of Medicine and

Cancer Centre in Marseille, then research officer at INSERM, consulting attaché in dermatology for the A. de Rothschild Ophthalmological Foundation in Paris, director of the Research Laboratory on Human Skin Tumours and the Research Group on UV Radiation and the Skin. His expertise lies in the fields of human skin pigmentation, skin cancer, particularly melanoma, the evaluation of sun protection products, the protection offered by clothing and optimization of natural defences against UV-induced oxidative processes. He is the founding chairperson of the NGO Sécurité Solaire, a WHO collaborating centre for communication on UV radiation. He is UV vice-chairperson for "interactions between optical radiation, skin and eyes" of division 6 of the CIE, a member of ICNIRP, an expert member of IEC TC 61 MT16, an expert member of CEN WG8 on "measurement of UV, visible and IR radiation" and presiding member of EUROSKIN. Member of the French Radiological Protection Society, non-ionizing radiation section. Dr Césarini has retired from clinical and research activities, but continues to serve as an expert for ICNIRP, the CIE, the IEC and the European Commission.

Jean Donadieu

Jean Donadieu is a doctor of medicine, a former intern in the Paris hospital system and former assistant chief resident in oncohematology. He practised in the regional hospital (CHR) in Orléans (1994) and served as attaché in the Hematology and Oncology Department of Trousseau Hospital (from 1996). His clinical research has focused on acute lymphoblastic leukaemia in children (analysis of data from the Fralle protocols). Establishment of a clinical research network on Langerhans cell histiocytosis and a clinical research network on congenital neutropenia. He served a limited term as research officer in INSERM unit SC 11 from November 2001 to December 2002 to establish an observatory on Fabry's disease and conduct epidemiological studies of two rare diseases (vernal keratoconjunctivitis and veinous and lymphatic malformations). Since 2003, he has been in charge of the medical ionizing radiation programme in the Health and Environment Department of the Health Watch Institute (InVS), with responsibility for referrals concerning veterans of nuclear testing and UV exposure.

Gilles Dixsaut (scientific secretary of the working group)

Gilles Dixsaut is a doctor of medicine, former faculty lecturer and fellow of the Paris hospital system. He is qualified in medical biology, specializing in functional exploration techniques. He holds an academic and research degree in human physiology (regulation of the internal environment). As an inspector-general of public health, after occupying various positions under the health department in the fields of scientific intelligence, technological forecasting and innovation, medical technology and environmental effects on health, he is currently head of the physical agents, new technologies and major facilities unit at Afsse. He is in charge of coordinating scientific evaluation of the risks of non-ionizing radiation in particular. He is chairperson of the health and biometeorology committee of the Higher Meteorological Council.

Christiane Guinot

Christiane Guinot is director of the Biometry and Epidemiology Unit of CERIES, a private centre for research on human skin funded by Chanel. In this post, she has been responsible for drafting, in conjunction with the team in charge of the SU.VI.MAX epidemiological study, some ten or so protocols on the determinants of skin condition and skin aging. She holds a doctorate in biomathematics (1982) and a research supervision accreditation (2003). She held a postdoctorate fellowship at the Institut Gustave Roussy (1982-84) and subsequently was a visiting research fellow at the Showa University Medical School in Tokyo as part of a scientific exchange between France and Japan (1984-86). On returning to France, she created and subsequently ran the Biostatistics Department for a pharmaceutical company belonging to the Rhône-Poulenc-Santé Group, followed by the Biometrics and Information Technology Department of RP-Tanabe (a European joint venture between Rhône-Poulenc-Santé and Tanabe Seyaku) from 1986 to 1991. She has served as vice-president of the French Statistical Society (2000-04), and she became a member of the International Statistical Institute in 2002 and a member of the board of overseers of the foundation "La Science Statistique" in 2004.

Marie-Aleth Richard

Marie-Aleth Richard is a doctor of medicine, professor and hospital attending physician. She holds a specialized degree in dermatology and venerology, a graduate degree in environmental chemistry and health (health option) from the Université de la Méditerranée in Marseille (July 1992), and a diploma accrediting her to supervise research (April 2000, Marseille Faculty of Medicine). In addition, she is a member of the French Dermatology and Syphiligraphy Society, a member of the International Dermato-Epidemiology Association (IDEA), a member of the French Dermatological Society's research group on bullous dermatitis, a member of the network for dermatological epidemiology, a research group of the French Dermatological Society, and a member of the College of Dermatology Instructors (CEDEF). Her research focuses on the epidemiology and care of melanocytic tumours.

Anne-Marie Dervault

Anne-Marie Dervault is a doctor of pharmacy and holds a postgraduate degree (DEA) in cutaneous biology (Faculty of Pharmacy, Paris XI, 1984) and a doctorate from Paris XI University in pharmaceutical sciences (1988). She is a Paris XI University Scholar and a winner of the Laboratoires Roussel prize (1988). She now works at Afssaps as a cosmetics evaluator.

Marie-Thérèse Leccia

Marie-Thérèse Leccia is a doctor of medicine and holds a doctorate in science. She serves as a professor and attending physician in dermatology in the multidisciplinary medical department of the Albert Michallon university teaching hospital (CHU) in Grenoble. Her research has focused primarily on ultraviolet radiation, and in particular on the protection offered by antioxidants against certain effects of UV radiation.

Béatrice Secretan

Béatrice Secretan, originally from Switzerland, studied biochemistry at the University of Geneva, then obtained a Master's Degree in chemical carcinogenesis at the Swiss Institute for Experimental Cancer Research at Epalinges sur Lausanne. She took her doctorate at St. Bartholomew's and the Royal London School of Medicine and Dentistry in London, UK in the toxicology department. Two grants from the National Scientific Research Fund and the Swiss Cancer League enabled her to work as a postdoctoral fellow at the Harvard School of Public Health in Boston, followed by a short stay at the UCLA School of Public Health in Los Angeles. She returned to Europe in 2001, joining the Gene-Environment Interactions Unit at the International Agency for Research on Cancer (IARC) in Lyon, France. For the last three years, she has worked in the Unit coordinating the IARC Monographs programme, where she is responsible for exposure data concerning the agents evaluated.

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Summary of report entitled

ULTRAVIOLET RADIATION

Current knowledge of exposure and health risks

May 2005

Introduction

Ultraviolet radiation is part of the non-ionizing electromagnetic radiation spectrum emitted by the sun, in the same way as visible radiation (light) and infrared radiation. Although ultraviolet radiation is invisible to the naked eye, the body reacts to it with protective mechanisms: darkening and thickening of the outer layer of the skin. As a result of its penetration into the skin and its mutagenic potential, exposure to ultraviolet radiation, whether natural or artificial, involves some major medium- and long-term health risks, especially for sensitive populations like children. The risks associated with exposure to UVB radiation have long been known, whereas the mutagenic activity of UVA radiation has been known for less than ten years.

The attention of the public authorities was first drawn to the risks associated with exposure to artificial ultraviolet radiation in 1995, and legislation was passed in 1997 (Decree no. 97-617 of 30 May 1997 relating to the sale and provision to the public of certain tanning devices using ultraviolet radiation, and its implementing orders).

Following a study of the mutagenic role of UVA radiation conducted by G. Halliday's team in 2004, Afsse informed the French Ministry of Health of its results in a note dated 19 April 2004, and added an FAQ section to its website in July 2004. The Health and Environment Ministers than requested Afsse (referral of 6 September 2004) to reassess the health risks associated with exposure to ultraviolet radiation of natural origin and with the use of tanning facilities. To reply to the questions posed by the Ministry's referral, Afsse set up a group of experts including representatives of the Academy of Medicine, IARC, members of Inserm research laboratories, and practitioners specializing in the field, as well as representatives of InVS and Afssaps, to which the referral was addressed.

As it is difficult to differentiate between the consequences of exposure to natural and artificial ultraviolet radiation in terms of overall effects, the experts' group decided to base its report on a global analysis of the UV risk. Thus in addition to the objectives stated in the referral, Afsse extended the study to include the possible risks associated with domestic use of "broad-spectrum" light bulbs which emit ultraviolet radiation in addition to the visible spectrum. The experts' group also considered the possible consequences of the use of sunscreens (mainly effective against UVB radiation), which can lead to longer exposure and therefore an increased risk associated with exposure to UVA radiation.

InVS and Afssaps were requested to deal with different aspects of ultraviolet radiation. In parallel to the referral to Afsse, a second working group was set up by InVS to characterize the exposure of the French population, while Afssaps issued a report entitled "Ultraviolet radiation and the use of cosmetic products". The proceedings of the various working groups are presented in a joint report.

The physics of ultraviolet radiation

Ultraviolet radiation is a portion of the non-ionizing part of the electromagnetic spectrum, situated in the wavelength interval between 100 and 400 nm. It is usually divided into three regions: UVA (315-400 nm), UVB (280-315 nm) and UVC (100-280 nm), and can be emitted by natural sources (solar radiation) or artificial sources.

The effective biological ultraviolet radiation (UVReff) at a given wavelength is the value of the energy level of the ultraviolet radiation multiplied by a specific efficiency factor of the biological effect in question at that wavelength. It is expressed as $W.m^{-2}$ (eff). The biological efficiency of ultraviolet radiation (E_{eff}) is used in standard IEC 60335-2-27 2002 to evaluate the emission limits of tanning devices.

The Standard Erythema Dose (SED) measures the erythemal UV radiation equivalent to effective exposure of 100 $J.m^{-2}$. The Minimal Erythema Dose (MED) is the dose that produces barely perceptible erythema (with clearly defined edges) in a given individual on a defined surface.
In 1997, the Erythemal Effectiveness Spectrum for human skin became an ISO/IEC standard, which allows the erythemal effectiveness of a given UV source to be calculated by convolution with the emission spectrum of that source. The ratio between the solar emission spectrum and the erythemal effectiveness spectrum is used to calculate the UV index, a tool designed for communication to the general public. It expresses the erythemal power of the sun (UV index = 40 x E_{eff} $W.m^{-2}$).

Limit values

The international scientific bodies responsible for the subject of exposure of workers and the general public (ACGIH and ICNIRP) have established the maximum daily doses that a worker exposed to UV radiation can receive without the risk of acute or long-term effects on the eyes. The maximum daily dose has been fixed at 30 $J.m^{-2}$ Eff, i.e. just under one-third of the SED. This dose takes account of the average cell repair capacity.

There are currently no recommended maximum limits for human skin, as the values established for ophthalmological risk take no account of the thickness of the skin and its thickening as a result of repeated exposure. The maximum limits recommended only constitute advice for indoor workers, and cannot be applied to outdoor workers.

The biological effects of ultraviolet radiation

Short-term effects of ultraviolet radiation		
Actinic erythema (sunburn)	- Its intensity and duration are proportional to the quantity of UV radiation received. - It appears a few hours after exposure to UV radiation, and culminates between 24 and 36 hours, then disappears on the 3rd day, to be replaced by marked pigment darkening - Possibility of fever, headache and vomiting, depending on the size of the damaged areas and the dose received.	UVB (E=5%) (E_{eff} = 80%) UVA (E=96%) (E_{eff} =20%)
Thickening of epidermis	- The keratinocytes in the basal layer actively divide around the 3rd day after irradiation. - This provides a degree of photoprotection. - Skin peeling allows a gradual return to normal in 5 weeks in the absence of new irradiations.	UVB
Immediate pigment darkening	- The melanins present in the melanocytes and keratinocytes polymerize; this leads to immediate pigment darkening, which is visible when irradiation ceases. - This is a temporary phenomenon. - This reaction is not developed by melano-compromised people.	UVA (10 J/cm²)
Adaptive pigment darkening (tanning)	- Visible on the 3rd day after irradiation, and persists for 3-4 weeks in the case of a single irradiation - In the case of repeated exposures, the pigment darkens increasingly, and this lasts for as long as peeling remains within normal limits. - Exposure to solaria: protection against solar radiation remains fairly low; much lower than that obtained, with an equal tan, from a series of exposures to the sun, as there is little thickening of the skin.	UVA UVB
Production of vitamin D by the skin	- This is a complement to vitamin D of food origin (80% of needs would be covered by a few minutes' exposure of a small part of the body twice a week). - Vitamin D is needed to fix calcium to the bone matrix. - A real deficiency can be observed in Nordic countries in people with phototypes V and VI, but eating foods rich in vitamin D can compensate for this deficiency. The risk of hypovitaminosis D observed in some populations no longer justifies exposure to artificial UVB radiation.	UVB
Phototoxicity and photoallergy	- The presence in the integument of endogenous substances (porphyria) or exogenous substances (medicines) can trigger phototoxic reactions which present clinically as severe sunburn. - Phototoxic reactions are theoretically restricted to irradiation and substance deposit sites. Photoallergic reactions, often eczematous, extend far beyond the irradiated areas. They require prior contact with the allergen.	
Keratitis and cataracts	- Inflammation of the cornea (keratitis) and temporary blindness (snow blindness) are observed a few hours after exposure. These symptoms are reversible in a few days, but can cause peripheral proliferations (pterygium) in the long term in the event of repetition. - In the long term, the cells constituting the crystalline lens are opacified (cataract) by UVA radiation, leading to a gradual loss of vision. - There is little risk of acute damage to the retina. However, observation of a bright light source can cause retina burning similar to that found in people who watch a solar eclipse without protection.	UVA UVB

	- In the long term, UV exposure may be involved in age-related macular degeneration.	

Genotoxic effects		
Photogenotoxicity	- An alteration in the chemical structure of the DNA can cause the appearance of mutations or lead to cell death (apoptosis). - Main types of damage caused by the UVB and UVA components of solar radiation to the DNA: breakage of the nucleotide chain, covalent adducts with proteins, and products of modification of bases. - The nature of the physico-chemical processes involved in the modifications caused by exposure to UV radiation depends on the wavelength of the incident photons.	UVA UVB
Skin photocarcinogenesis	- Mainly comprises basal-cell carcinoma (BCC), featuring slow development and local malignity, and squamous-cell carcinoma (SCC), which is more aggressive. - Main risk factor: intermittent, "burning" solar exposure, especially during childhood, for melanoma and BCC. It is acknowledged that SCC is associated with chronic exposure. - The genetic susceptibility and mechanisms involved in the photocarcinogenesis of melanomas and carcinomas are very different. - The roles of the different wavelengths of the solar spectrum also differ, according to the nature of the cancer.	UVA (35%) UVB (65%)
Immunosuppressive effects		
The skin's immune defences protect against external aggression (bacteria, fungi and viruses). These defences are considerably impaired by weak doses of UVB and UVA (below the erythemal dose). This depression is reversible, and its restoration takes around 3 weeks. Following exposure to solaria, the skin's defences are lowered, and skin infections have been observed in tanning centres with poor hygiene.		
Photo-induced skin aging (heliodermatitis)		
Mainly observed in uncovered areas: the face (nose and cheeks), back of the hands and forearms. It varies considerably from one person to another, and even between people of the same age and phototype who undergo the same chronic solar exposure (thus indicating individual genetic susceptibility). The histological modifications concern the epidermis and dermis, but the dermal connective tissue and its cells are the preferential target of solar radiation. UVA radiation, which penetrates deeply into this tissue, plays a large part in forming these lesions.		
Photo-induced skin cancers		
Some 80,000 new cases of skin cancer are diagnosed in France every year. The number is constantly growing, with an annual increase of 7 per cent. Ultraviolet radiation is the major aetiological factor responsible for these cancers, whose aggressiveness depends largely on their histological form. The process of cancerization is the result of damage caused by UV radiation accumulated in the epidermal cells.. The mutagenic and carcinogenic effects of UVB radiation in animals and humans have long been known, whereas the oncogenic effects of UVA radiation have only been recognized for a few years. The carcinogenic risk of UV-emitting tanning devices is therefore a topical subject, which can be considered a public health problem.		
Skin carcinomas	- basal-cell carcinoma (60%): slow malignant extension, purely local (no metastasis) - squamous-cell carcinoma (30%): occurs on existing lesions (actinic keratosis, leucoplakia of the lips)	UVA (35%) UVB (65%)
Skin melanomas	- Risk factors: solar exposure, genetic (fair skin, failure to tan easily, blond or red hair, etc.), number of moles, family history of melanoma, high solar exposure during childhood	UVA UVB
Ocular melanoma		
Some publications have suggested a positive correlation between the onset of ocular melanoma and exposure to UV radiation. A recent French publication (relating to workers) seems to confirm this correlation.		

Health effects of ultraviolet radiation

Characteristics of phototypes:

Phototype	Hair	Complexion	Freckles	Sunburn	Tan
I	Red	Milky	+++	Always ++	0
II	Blond	Pale	++	Always +	Slight tan
III	Light brown	Pale	+ or -	Frequent	Pale tan
IV	Dark brown	Dark	0	Rare	Dark
V	Dark brown	Dark	0	Exceptional	Very dark
VI	Black	Black	0	None	Black

Data specific to the French population

° A specific study was conducted in 1998 on the SU.VI.MAX cohort (however, this cohort cannot be considered really statistically representative of the French population):

Phototype I	0.3%
Phototype II	13%
Phototype III	46.4%
Phototype IV	34.2%
Phototype V	6.1%

° According to a recent case-control study (Bataille et al. 2005, in press):

Phototype I	11.6%
Phototype II	25.7%
Phototype III	30.9%
Phototype IV	31.5%

Epidemiological studies – natural ultraviolet radiation

The population receives 3 to 6 per cent of ambient ultraviolet radiation in temperate countries. Some examples of annual exposure:

Office workers	200 SED (exposure at weekends and holidays) = 3-6% of total ambient UV radiation (temperate countries)
Children under 18 years old	300 - 400 SED
Outdoor workers	400 - 800 SED

Melanins and photocarcinogenesis

Epidemiological analysis of skin cancer (melanoma, basal-cell carcinoma and squamous-cell carcinoma) shows that predominantly phaeomelanic (red-haired) populations form the majority of skin cancer sufferers (IARC, 1992).

Skin cancer

The various types of skin cancer, i.e. melanoma and non-melanoma skin cancers (basal-cell and squamous-cell cancers, described as epidermoid carcinomas by French authors), are now the most frequent types of cancer, and their frequency is increasing among all fair-skinned populations, reaching epidemic proportions. In Europe, it is estimated that although the population of the European Union (25 member states) will remain constant between 2000 and 2015, a 22 per cent increase in non-melanoma skin cancer in persons aged over 65, and 50 per cent in those aged over 80, is to be expected (Boyle et al., 2003).

Basal-cell and squamous-cell cancer (often collectively described as non-melanoma skin cancers) are the most frequent types of cancer. Basal-cell carcinoma is around four times more frequent than squamous-cell carcinoma, and both are 18-20 times more frequent than melanoma. However, the incidence estimated by surveying a population is much higher than that recorded in the registers. The total of 80,000 cases of non-melanoma cancer is therefore probably significantly underestimated, as numerous skin tumours, especially basal-cell and squamous-cell carcinoma *in situ*, are destroyed without histological analysis.

Non-melanoma skin cancer

The epidemiology of non-melanoma skin cancer is far less well known than that of melanoma. In particular, only a little data has been systematically collected from populations.

Epidemiological studies (descriptive studies, cross-sectional studies, case-control studies and cohort studies) of non-melanoma skin cancer are analyzed below.

- Skin cancer mainly affects fair-skinned populations. Non-melanoma skin cancer mainly affects parts of the body chronically exposed to sunlight, such as the head and neck. However, a special feature of the anatomical distribution of basal-cell cancer is that it is almost absent from the back of the hands, and rare on the forearms. This cancer also affects parts of the face which receive relatively little light.
- Since the late 1930s, the incidence and mortality of non-melanoma skin cancer has been inversely related to latitude, i.e. proximity to the equator.
- There is an association with local levels of UV irradiation and studies of immigrants to Australia show that migration from a less sunny to a more sunny country is associated with increased risk.
- There is an association between the risk of non-melanoma skin cancer and outdoor employment.
- Several transverse cross-sectional studies conducted in Europe, Australia and the USA have analyzed a number of sun exposure parameters (job, leisure exposure, sunburn, actinic lesions) in different populations. These studies show that the risk of squamous-cell skin cancer is multiplied by a factor ranging between 1.7 and over 3, depending on the degree of exposure and the exposure parameter.

- 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 squamous-cell cancer, but no correlation between the accumulated dose of sun exposure and the risk of basal-cell cancer. Conversely, the risk increases with recreational exposure during childhood and adolescence, and the more sensitive an individual is to the sun, the higher the risk will be.

Melanoma

In 2000, an InVS study estimated the number of new cases of cutaneous melanoma which had appeared in France at 7,231: 42 per cent in men and 58 per cent in women. However, the 95 per cent confidence interval is wide: 6,132-8,330 cases, because the estimate is based on registers which only cover part of the French population. Cutaneous melanoma is believed to have been responsible for 1,364 deaths in 2000, 704 of them in men (52 per cent), 47 per cent of whom died before reaching the age of 65. The number of deaths is known with a fairly high degree of precision.

Melanoma is one of the tumours whose incidence is increasing most. In France, between 1978 and 2000, the incidence increased by 5.9 per cent per annum in men, and mortality by 2.9 per cent per annum. In women, the incidence increased in the same period by 4.3 per cent per annum, and mortality by 2.2 per cent per annum. A man born in 1953 is ten times more likely to suffer from cutaneous melanoma than one born in 1913, while the factor is six to one for women. The net risk for a man of dying of cutaneous melanoma is multiplied by 2.7 between these two cohorts, while the risk is multiplied by 2.1 for women. In view of this rate of progress, the incidence of melanoma in 2005 can be estimated at 8000.

The individual risk of melanoma is influenced by host factors (pigmentation characteristics, reaction of skin to sun) and an environmental factor: sun exposure. Sun exposure is now considered to be a leading cause of melanoma. Studies conducted in the 1980s established a correlation between sun exposure and the risk of melanoma, but it is not a simple one. The total accumulated dose of solar radiation is not the only factor involved, and the type of sun exposure, according to age, plays an important role. Moreover, although the ultraviolet component of the solar spectrum seems to contribute to inducing melanoma, the ultraviolet wavelength(s) which contribute to the development of melanoma are not yet definitely known.

The conclusion that solar radiation causes melanoma is based on:
- the positive association between melanoma and residence at low latitudes;
- arguments drawn from studies of migrants, which indicate that the risk of melanoma is associated with exposure to sunlight in the place of residence in early life;
- the anatomical distribution of melanoma, which is more frequent in skin regions regularly or usually exposed to the sun, especially intermittently;
- findings drawn from case-control studies and cohort studies which indicate that melanoma is associated with residence in hot climates, is correlated with solar skin lesions, and is positively associated with intermittent sun exposure and a history of sunburn.

There is currently a fairly broad consensus that melanoma is caused by exposure to solar ultraviolet radiation. Armstrong and Kricker (1993) estimate that 67-97 per cent of melanoma in different populations is attributable to sun exposure. Recent epidemiological studies in the USA and Europe indicate that the development of moles (a lesion indicating the risk of melanoma) in children and the development of melanoma are influenced by short periods of intense UVB exposure (Autier et al., 2003, Fears et al. 2003). However, it is not impossible that exposure to UVA radiation plays a part in the development of melanoma (Armstrong, 2004).

Exposure to ultraviolet radiation may also play a part in the growth and tumoral progression of melanoma. Exposure to ultraviolet radiation causes local and systemic immunosuppression, which may be involved in promoting the growth of melanoma and non-melanoma cancer. An odd phenomenon is the existence of seasonal variations in the incidence of melanoma, with the peak incidence in summer. These variations, which have been known for some 20 years, have been observed in several populations and in both hemispheres, and no clear explanation has yet been given.

Exposure to sunlight, and especially intermittent recreational exposure, is the main known risk factor for melanoma. However, it has been known for some 20 years that sun exposure can also affect the survival of melanoma patients. These findings suggest that sun exposure may increase the melanoma survival rate, but may also be explained by an association between incidence and early detection of melanoma. The mechanism of this effect is not known, but it illustrates the possibility that several pathways exist in the malignant transformation of melanocytes.

Other cancers

A number of ecological studies have suggested that intense sun exposure is liable to interfere with the incidence or mortality rate of some types of cancer, especially breast, colon, and prostate cancer and lymphomas. These rather surprising results need to be confirmed by new studies which take full account of sun exposure, supported by studies of the mechanisms involved.

Epidemiological studies – artificial UV radiation

A UV tanning session corresponds to exposure of at least 2 SED. In practice, one session corresponds to approximately 1 MED, i.e. for phototype II = 3 SED, phototype III = 5 SED and phototype IV = 7 SED.

Risk of skin cancer based on number of annual sessions in a 10-year period:

- 10 sessions: risk multiplied by 1.03
- 30 sessions: risk multiplied by 1.10
- 100 sessions: risk multiplied by 1.39
- 300 sessions: risk multiplied by 2.73.

Melanoma

The risk factors are now well established: pale skin, number of naevi > 50, repeated sunburn (Gallagher et al., 2005).
Epidemiological studies, and especially a meta-analysis and a cohort study (Veierød et al., 2003), have found that the use of tanning devices increases the risk of skin melanoma by a factor of between 1.25 and 1.50. This risk increases with the frequency and duration of use, and is most marked when the exposure takes place in a young adult. It should be noted that a modest but significant increase in risk may lead to a major increase in the number of patients, due to the frequency of use among the population, as the use of artificial tanning is becoming increasingly popular. Exposure to artificial ultraviolet radiation may double the annual doses received in some areas (face, neck, arms, legs, etc.).

Basal-cell and squamous-cell carcinoma

A number of case studies have linked exposure to artificial UV radiation to skin cancer, but very few case-control studies have explored the relationship between exposure to tanning devices and the risk of basal-cell and squamous-cell skin cancers. The only meaningful results are the findings of a 2002 American study, which showed that the risk that users of artificial tanning devices will develop squamous-cell skin cancer is multiplied by 2.5, and the risk of developing basal-cell skin cancer is multiplied by 1.5 (Karagas et al., 2002). As in the case of melanomas, the risks increase when the first exposure occurred at a younger age. These results suggest that the use of tanning devices is a risk factor for non-melanoma skin cancers.

Other effects of UV radiation

Effects of UV radiation on skin aging

Little is known about the skin condition of the populations of the industrialized countries, even though, in terms of public health, skin diseases are responsible for major morbidity. Chronic exposure to sunlight, or to other environmental factors such as cigarette smoke, frequently has repercussions on the skin, commonly known as photo-aging, that vary with anatomical location, total exposure time and phototype. The results of a French study published in 2000 (Malvy et al., 2000) suggest that the prevalence of skin photo-aging in the overall adult French population is determined by age, sex, phototype, region of residence and, for women, by menopausal status. Histologically observed actinic elastosis indicates actinic skin aging.

Photodermatitis

Photodermatitis is a general term for all skin diseases involving photosensitivity, i.e. in which the skin shows abnormal reactions to light and UV radiation. Photobiological exploration can help diagnose the type of photodermatitis, detect the wavelength(s) involved in the disorder, and identify any product or agent involved in the reaction.

Effects of UV radiation on the eye

In adults, the cornea of the eye absorbs all UVC and most UVB radiation. UVA radiation passes through the cornea and is absorbed by the crystalline lens. Visible light and infrared radiation reach the retina.

The acute risk of ultraviolet radiation and visible light for the eye:

- Acute keratoconjunctivitis: This condition appears following unprotected exposure to sunlight (particularly when the sun's radiation is reflected by snow, sand or cement) or to artificial light such as that of welding arcs, high-pressure discharge lamps and sunbeds. The symptoms of "arc flash" and "snow blindness" are tearing, redness and intense pain in the eyes, difficulty in keeping them open in the presence of light (photophobia) and a feeling of having sand in one's eyes.
- Acute solar retinopathy: Acute solar retinopathy occurs after looking at the sun (e.g. during observation of eclipses) or after prolonged exposure to sunlight without eye protection. Sources of intense artificial light such as welding arcs and some surgical microscopes can also damage the retina.

UV radiation can cause other lesions in some subjects in the long term:

- Cataracts: Epidemiological studies, some of which involved over 100,000 people, give reason to think that cataracts may be directly linked to UV exposure. This research demonstrated, among other things, that areas receiving considerable UV radiation show a high prevalence of cataracts.
- Senile macular degeneration (SMD): This frequent disease of the retina currently affects one of every four people in the 75-85 years age group. It causes partial but virtually incurable blindness by cutting out the centre of the field of vision. Repeated exposure to solar radiation (visible + UV) may lead to SMD. A recent epidemiological study (Tomany et al., 2004) of a cohort of over 6,000 individuals seems to establish a link between SMD and prolonged exposure to the sun (particularly during adolescence) and suggests that the risk is reduced by over 50 per cent if individuals protect their eyes by wearing sunglasses and hats, caps or visors.

Behaviour and exposure

Exposure to natural UV radiation

Satellite observation

Since 1985, the SoDa programme (www.soda-is.com) has been using observations by meteorological satellites to measure the solar radiation received at ground level. The advantage of this system is the complete coverage of France's national territory by its grid, and the ease of measurement it offers. As the archive is currently limited to 21 years, however, it does not allow calculation of variations in UV exposure in relation to climate change.

Ground-level observation

Two stations in France (Lille-Villeneuve d'Ascq and Briançon) are currently equipped with UV spectroradiometers, which are recalibrated regularly and have participated successfully in several European campaigns. These two stations for spectral measurement of solar UV radiation operate as a network with the following purposes: a) to study the natural variability of this radiation and the various parameters that modulate it; b) to detect any long-term trends; c) to provide spectral UV data allowing validation of climatologies based on satellite observation; d) to make this data available to various communities of potential users.

Sécurité Solaire data and the MOCAGE model: sequential monitoring of exposure based on meteorological satellites

This is an application of the MOCAGE (MOdèle de Chimie Atmosphérique de Grande Echelle – Large-Scale Model of Atmospheric Chemistry) project. This model, which is already operational, forecasts UV indexes which are announced to the media by Sécurité Solaire.

Convergence and complementarity of information between this system and other measuring systems has not been studied.

Human behaviour with respect to natural UV radiation: review of the French data

Most of the information available to date comes from studies of the populations of other Western countries (Australia, Canada, Great Britain, the Scandinavian countries), which also provide methodological principles and comparative data. The French data is rather limited.

The SU.VI.MAX cohort:

The SU.VI.MAX cohort is a national cohort of volunteers participating in a controlled trial concerning food supplements, which includes an arm relating to studies of exposure to ultraviolet radiation. This study supplies information about the phototype of the population and analyzes behaviour by classifying individuals on the basis of their sun protection and exposure habits. The limitation of this national cohort in terms of knowledge of UV exposure lies in its demographic representativity, as all volunteers belong to the generations born between 1930 and 1960.

Montpellier child study

A 1993 study, based on a self-administered questionnaire, of 573 children aged 3 to 15 in the Montpellier area, sought information on exposure to the sun during the summer of 1992. Exposure to UV radiation during the summer was considerable, exceeding 6 hours per day in some cases, which for an entire summer amounts to 366 hours of median exposure. This one-off study was not repeated, and no other geographical areas have been covered.

Health Examination Centres study

This was a national study conducted in 2001 on a sample of 33,021 individuals aged

over 30 years old, resident in France, during a randomized multicentric interventional trial for prevention and early diagnosis of skin cancer in health examination centres. This study mainly provided information on how informed the adult population is concerning exposure to the sun. It was not intended to collect information on exposure itself, nor to determine the time budget of those surveyed with respect to UV exposure.

Exposure to artificial UV radiation

Information on exposure to artificial UV radiation is highly fragmented in France. In practice, only two studies estimate such exposure: a) the SU.VI.MAX study, which found that 22 per cent of women and 8 per cent of men have used a tanning device, and b) the Health Examination Centres Study, which showed that 2 per cent of subjects frequent tanning booths. The financial data for the industry does not allow analytical examination of this business, which according to manufacturers is growing.

Conclusions of studies on human behaviour with respect to UV radiation in French population groups

To date, there are no general studies of the French population, covering all age groups, on human behaviour regarding natural or artificial UV radiation. The studies that have been conducted have served to validate the questionnaires and a methodology. The behaviour of teenagers and young adults, however, is entirely beyond the scope of these studies, although these age groups are a commercial target for tanning booth businesses and are important for campaigns aimed at better informing the public about the risk of UV radiation. Although childhood is the period of life when intense exposure may have a substantial impact on the subsequent risk of cancer, the only study available on this aspect dates from 1993.

UV exposure and occupation

There is little documentation on work-related exposure to UV radiation. An evaluation of such exposure by occupation was made as part of an epidemiological study on ocular melanoma. In the absence of usable data from measurements, UV exposure was evaluated on the basis of the judgement of industrial health experts.

Exposure to natural UV radiation (outdoor occupations)

Outdoor occupations involve exposure to solar UV radiation. The intensity and frequency of such exposure may differ substantially between individuals having the same occupation, depending on local circumstances or the individual's activities. Seamen and fishermen are particularly exposed to this risk, as are mountain guides, ski instructors, swimming instructors, lifeguards, construction workers, etc.

Exposure to artificial UV radiation

Some occupations can involve exposure to artificially produced UV radiation. The spectrum of artificial UV radiation can be substantially different from that of solar UV radiation. In particular, it can include UVC radiation (arc welding), which is especially harmful.

Cosmetic products and UV radiation

Sun protection products

Current scientific knowledge indicates that sun protection products effectively protect against erythema (sunburn). This protection is necessary, but insufficient. There is no parallel between the acute effects of ultraviolet radiation, especially erythema, and its chronic effects, because their biological mechanisms are different. The disappearance of sunburn due to the use of sun protection products consequently does not guarantee an equivalent reduction in skin aging and the risk of cancer.

The acute toxic effects of sun exposure, especially erythema, are associated with the dose received, and also with the dose rate; the more intense the ultraviolet radiation, the greater the risk of sunburn. Sunscreens reduce the intensity of the radiation that penetrates into the skin, and therefore the dose rate and the risk of sunburn. The chronic toxic effects of sun exposure (skin aging, actinic keratosis and squamous-cell carcinoma) are the consequence of the total cumulative dose of ultraviolet radiation absorbed by the skin. If sun protection products are used to sunbathe for longer, the total dose absorbed by the skin will be very high, and may be even greater if no warning is given by sunburn.

The quantity of ultraviolet radiation that penetrates into the skin, after application to skin protected by a sun protection product, is reduced by a percentage that varies according to the value of the protection factor (PF) (sun protection factor = $MED_{protected}/MED_{unprotected}$). For example, a product with a factor of 10 blocks 90 per cent of UVB radiation, but allows 10 per cent to pass through permanently. Thus if the dose received by the skin is equal to the MED, sunburn will appear, and the more intense the solar radiation the more rapidly it appears, despite re-application of the product. For a person with a fair phototype (who sunburns after approximately 20 minutes) using a sun protection product, this corresponds to the onset of erythema after 3 hours' exposure in the South of France in June, or one hour's exposure in the tropics.

Thus the incorrect use of a preventive measure can increase the risk by suppressing warning signs. Information about the correct use of sun protection products should therefore emphasize the fact that these products are designed to protect the skin under normal exposure conditions, but do not allow the time of exposure to be increased under any circumstances.

Risks related to the association of UV radiation with cosmetic products other than sunscreens and dietary supplements

The pathologies classified under the general term "photosensitivity" are associated with abnormal skin reactions to radiation in the UV and visible spectra. These reactions may be caused by either sunlight or artificial light sources, and they present a great variety of clinical symptoms. Photosensitivity conditions may be divided roughly into two groups: genodermatitis, and photosensitive reactions to certain chemical and pharmaceutical

products. In addition, many pathological conditions may be exacerbated and in some cases triggered by UV radiation. Photosensitive reactions due to chemical products, either systemic or topical, represent a problem of growing importance, as new products are constantly arriving on the market. Once these agents penetrate the skin, they may absorb radiation and trigger an abnormal reaction. The reactions induced by UV radiation may be phototoxic, i.e. capable of affecting the entire population if the agent is provided in sufficient quantity, or linked to a biochemical and immunological reaction, which affects only part of the population. However, both types of reaction may be triggered simultaneously by the same molecule in the same individual.

International, European and national positions concerning UV-emitting appliances

Appliances designed specifically for tanning were defined in an international standard prepared by the International Electrotechnical Commission (IEC). This standard came into effect in 1985 and was amended in 1990 and 1995 (IEC standard 60335-2-27). It classifies UV-emitting appliances under four types, depending on the power of the UVA and UVB radiation emitted.

Pursuant to article 5 of Directive 73/23/EEC (the Low-Voltage Directive), the European Commission considers that the legislation governing the safety of UV tanning devices used for cosmetic purposes (harmonized standard EN 60335-2-27: 1997) is insufficient. The Commission consequently requires appliances to be adapted to conform to the harmonized standard, which will prevent changes to the international standards after 1997 (especially the 4th edition, and its amendments 1 and 2) from being taken into account in the drafting of European standards.

A joint public health opinion issued by the radiological protection and health authorities of five Nordic countries (Sweden, Finland, Norway, Iceland and Denmark) in 2005 recommends, in keeping with the positions of international (WHO, ICNIRP, 2003), European (EUROSKIN, 2000) and national bodies (the French Academy of Medicine, the French Dermatological Society, etc.), that increased safety precautions be taken in the use of UV-emitting tanning devices.

As regards legislation, France has passed Decree no. 97-617 dated 30 May 1997 relating to the sale and public availability of certain tanning devices that use ultraviolet radiation. The Decree is supplemented by three executive orders. The important points of Decree no. 97-617 may be summed up as follows:

- The classification of appliances follows that of the 1995 IEC 60335-2-27 standard. Only type 1 and 3 UV appliances are permitted.
- It excludes phototype I subjects and minors from using these appliances.
- It provides for specific training for operators, who must always be present when tanning sessions are in progress (automatic, self-service machines are excluded).
- It provides for mandatory declaration of UV appliances to the Prefect, and an initial inspection of appliances, followed by inspections every two years. The technical regulations that certified inspection bodies are required to follow are set out in a circular.

Conclusions

Conclusions of Afsse experts' group

Exposure to UV radiation has a beneficial effect on human health, but the dose of UVB radiation necessary and sufficient for vitamin D synthesis is well below 1 MED per week. Exposure to UV radiation also has harmful effects, in both the short and long terms, on the skin, eyes and immune system.

Exposure to UV radiation is carcinogenic for human beings. This effect has long been known for UVB radiation, whereas the mutagenicity of UVA radiation has been demonstrated more recently.

Exposure to solar UV radiation is the main environmental cause of both non-melanoma skin cancer and melanoma. Prevention of skin cancer requires reduction of exposure to the sun. Furthermore, the recent publication of epidemiological studies which indicate a higher survival rate when the skin adjacent to the melanoma presents elastosis lesions, or a reduction in certain tumours (lymphomas) associated with exposure to the sun, do not justify the withdrawal of the recommendation in the European Code against Cancer to avoid excessive exposure to the sun.

It was long believed that UVA radiation presented no danger to health, and could be used as a tanning aid. We know today that this is not true, and that the UV doses received during artificial tanning sessions are added to those received during natural UV exposure, thus increasing the risks. Some epidemiological studies have failed to demonstrate the existence of a major risk. However, the recent publication of a meta-analysis of nine case-control studies and of a very large prospective cohort study allows us to assert today that tanning through exposure to artificial UV radiation increases the overall risk of melanoma by a factor of 1.25, i.e. an increase of one fourth. This risk is further increased by early or frequent exposure (by a factor of 1.6 to 1.7, and in the case of women who engaged in artificial UV tanning from 20 to 29 years of age an increase of 160 per cent). Furthermore in 2002, an American study showed that the risk that users of artificial tanning devices will develop squamous-cell skin cancer is multiplied by 2.5, and the risk of developing basal-cell skin cancer is multiplied by 1.5. Increased use of artificial UV radiation for tanning purposes is therefore a source of concern in terms of public health.

As regards the establishment of limit values on emission and exposure for carcinogenic risks, the proportionality between the erythemal effectiveness spectrum and the carcinogenic effectiveness spectrum is fairly good, so it does not seem necessary to introduce multiplication of the action spectra. The erythemal effectiveness spectrum may thus be considered as representative of all effects.

The use of sunlamps that only emit UVA radiation in tanning devices is inappropriate from the health standpoint. All suntanning is a response to aggression by UVA and UVB radiation, and the most recent studies have demonstrated that UVA radiation induces mutations and cancer. In addition, it is mainly UVA radiation that causes

photoaging.

There are a number of medical reasons for the prohibition of cosmetic products in tanning booths:

- The application of water/oil or oil/water preparations on the stratum corneum and the epidermis induces increased penetration of UVA and UVB radiation.
- Topical preparations can convey photosensitizing, phototoxic or photoallergenic substances that cause abnormal reactions, increasing the genotoxicity of UV radiation.
- Any use of topical products containing photoprotective agents, such as UVB or UVA filters, changes the radiation received by basal-layer cells in an unpredictable and potentially dangerous manner.

As regards the use of antioxidant preparations or taking oral products intended to protect or restore the natural defensive capacity of the epidermis, the results obtained to date are too fragmented and incomplete to allow us to recommend such practices during exposure to natural or artificial UV radiation.

The experts' group adds its voice to the many warnings and negative judgements concerning tanning by artificial sources issued by a variety of national and international public health bodies (WHO, ICNIRP, EUROSKIN, NRPB, France's National Academy of Medicine) and unequivocally advises against the use of UV tanning devices. In addition, the experts' group wishes to retain the classification of UV-emitting appliances used for tanning purposes as set forth in the NF-EN-60335-2-27 standard, 4th edition, 2000.

Conclusions of the InVS experts' group

Three complementary sources of data are currently available for measuring the natural (environmental) exposure of the French population to UV radiation.

- The European SoDa programme measures solar radiation at ground level through observations made by meteorological satellites, and estimates the proportions of UVA, UVB and erythemal UV in solar UV radiation for France's entire territory, divided into squares 5 km to a side. It provides a daily, monthly and annual database dating back to 1985.
- Two ground-level solar ultraviolet radiation spectral measuring stations in Lille-Villeneuve d'Ascq and Briançon-Villard St Pancrace are equipped with UV spectroradiometers which record the spectrum of total solar UV irradiance at 30-minute intervals. The scientific purposes of these two measuring stations, which operate as a network, are to study the natural variability of this radiation and the parameters that modulate it, to detect the long-term trends, and to provide spectral UV data allowing validation of climatologies based on satellite observation and for biological, medical and atmospheric chemistry applications.
- Lastly, Météo France and Sécurité Solaire publish projections of the UV index (a general indicator of solar UV radiation) for metropolitan France from May to October.

Considering the impact of intermittent exposure and the role of exposure in childhood, information on human behaviour with regard to UV radiation is very important in the analysis of UV risk. Most of the information available today stems from studies of Western countries' populations (Australia, Canada, the United Kingdom, and Scandinavia). The data on the French population is somewhat limited, and mainly based on three studies:

- The SU.VI.MAX cohort, a national cohort of 12,741 volunteers participating in a controlled trial of dietary supplements. The cohort has provided information on the skin phototypes found in France and the subjects' behaviour with regard to UV exposure: 22 per cent of women and 8 per cent of men reported that they had used artificial UV radiation.
- A 1993 cross-sectional study, based on a self-administered questionnaire, of 573 children aged 3 to 15 in the Montpellier area, which estimated the exposure to UV radiation over the summer.
- A national study, conducted during a randomized trial for prevention and early diagnosis of skin cancer in Health Examination Centres. This cohort of 41,143 adults over 30 years of age provides information on adults' attitudes with regard to exposure to the sun, but was not intended to collect information on exposure itself. In this study, 2 per cent of subjects reported that they use sunbeds, but this figure needs to be measured more accurately.

Individual dosimeters allow direct measurement of the UV dose received, in addition to the data from questionnaires, and have been used to measure the exposure received by children or adults in ordinary daily activities or on holiday. Although certain studies included French subjects, no study to date has measured the long-term exposure of the French population to natural UV radiation.

In conclusion, to date there are no general studies of the French population, covering all age groups, on human behaviour with respect to natural or artificial UV radiation. The behaviour of teenagers and young adults is entirely beyond the scope of these studies, despite the fact that these age groups are a commercial target for tanning businesses and are important to campaigns aimed at better informing the public about UV risk.

Work-related exposure to UV radiation is not well documented on the whole. It has been evaluated by determining indices of exposure to natural and artificial ultraviolet radiation for each occupation. Outdoor occupations involve exposure to solar UV radiation of an intensity and frequency which vary greatly from one occupation to another and between individuals having the same occupation. Seamen, fishermen and mountain guides are particularly exposed occupational categories. Some occupations can involve exposure to artificially produced UV radiation. This artificial UV radiation can be substantially different from solar UV radiation. In particular, it can include UVC radiation (e.g. arc welding), which is particularly harmful.

Recommendations

Recommendations by the Afsse experts' group

1. Exposure to the sun

Ultraviolet radiation plays a vital role in life on earth, yet exposure to solar UV radiation is the primary cause of skin cancer (the incidence of which is rising in a great many countries) and a major cause of cataracts. The health authorities should introduce measures to reduce the risks of exposure to both natural and artificial UV radiation to improve the health of the populations for which they are responsible.

The health authorities can make a significant contribution to reducing exposure to ultraviolet radiation by creating shady areas at bus stops, playgrounds, rest areas and schools, encouraging photoprotective measures in schools and recreation centres, inducing responsible behaviour on the part of businesses providing access to tanning devices or to natural solaria, and providing plentiful information liable to influence the public's knowledge and behaviour via the media.

Within the general population, children should be specifically targeted, as they spend more time outdoors than adults and are more at risk of the carcinogenic effects of UV radiation. The development of good habits in childhood helps substantially in ensuring regular use of suitable photoprotection in adulthood.

A preventive approach

- Increased use of the UV index

Efforts to inform the public can be based on more widespread use of the UV index, a simple indicator of solar intensity. These projections, made by the national meteorological agency, should be extended to areas offering tourist activities, summer resorts in the mountains, public swimming pools, amusement parks, etc. Better knowledge of the UV index and the personal protection methods associated with different levels would certainly influence people's behaviour and make it possible to reach them with simple messages on the prevention of skin cancer.

- Preventing photo-induced skin cancers

As excessive exposure to the sun plays a fundamental role in initiating and promoting skin cancer, so prevention necessarily involves reduced exposure to the sun from the earliest childhood years.
The aim is not to impose sweeping photoprotection measures on the entire population and throughout life, but rather to inform our fellow citizens about the dangers of UV radiation and to advise them as to ways of protecting themselves from it, particularly for individuals in the paler phototypes, people with many naevi and people exposed to intense sunlight.

The medical and paramedical professions are the best placed to deliver messages on primary prevention, many of which are simply commonsense advice: teach people how to assess their own skin's sensitivity to sunlight, remind them that they should avoid the hours when sunlight is most harmful (between noon and 4 p.m. in summertime), make clothing the first line of defence (tightly-woven cotton clothing provides simple,

inexpensive protection), recommend the use of topical photoprotection, with the aim not of increasing the number of hours of exposure but of protecting skin areas that cannot be protected by clothing, limit exposure to artificial UVA radiation, and prohibit minors from using sunbeds.

Protective sunglasses are recommended from an early age during sports and outdoor activities. The material should be suitable for children and ensure sufficient UV filtration.
The foremost target of primary preventive education should be parents, not only because they can control how much their children are exposed, but also because they can serve as an example for adolescents (who are exposed far too much) and give them advice. Photoprotective measures should begin in the earliest years of childhood, as the habits developed in childhood will then have every chance of persisting into adulthood.

- Attract the attention of the resident population and tourists

- The attention of the resident population and tourists should be attracted by billboards carrying photoprotection messages and distribution of information leaflets in busy areas and areas where the risks of overexposure are high (stadiums, training grounds, public swimming pools, parks and gardens, the seaside, etc.).

- Educational strategies

As regards education, a multidisciplinary approach to sun protection should be encouraged at all educational levels. It is important to inform the staff in charge of outdoor activities, educate people who run activities for children, adolescents and adults, and encourage parents to follow the recommendations of the sun protection programme before children go to school or leave for outdoor activities. Information about sun risk prevention should be given in schools.

Proper use of sun protection

The experts' group recommends effective use of sun protection items, but this term must not be taken to mean topical UV filters alone. Sun protection involves a number of measures designed to reduce exposure to ultraviolet radiation:

- Stay in the shade.
- Limit exposure during the hours when the sun is near its zenith (noon-4 p.m.).
- Wear protective clothing.
- Wear a wide-brimmed hat to protect eyes, face and neck.
- Protect your eyes with wrap-around sunglasses complying with the recommendations of the European Commission.
- Use topical sun protection products with a protection factor of 15 or higher on areas not protected by clothing.
- Keep children under one year of age out of the sun.

Draft recommendations concerning the labelling of sun protection products are being

developed by Afssaps. This project is designed to harmonize the methods of evaluation and labelling of sun protection products, simplify technical information, classify products in a limited number of categories to facilitate choice by consumers, and provide information on proper use of sun protection products to consumers.

2. Tanning facilities

The UV radiation received in tanning sessions is added to natural UV radiation, and thus contributes to skin photocarcinogenesis. There is no proof that the use of artificial tanning devices is less dangerous than exposure to the sun; it is therefore recommended that people should not expose themselves to artificial UV sources.

Considering that exposure to UV radiation in general should be limited, the use of UV tanning devices for other than medical purposes cannot be recommended. However, if they are used, the experts' group considers that it is necessary to limit the risks for users by limiting the annual UV doses and providing users with all the information they need to reduce skin damage and all other health risks[1]. In addition, it is important that tanning device operators be sufficiently well acquainted with the risks associated with UV radiation to help users reduce their personal risk and to avoid improper use of the appliances. In view of the importance of this personalized advice and of direct control, the use of automatic appliances is not acceptable under any circumstances.

The experts' group recommends that people aged under 18 and those who are particularly sensitive to ultraviolet radiation (skin phototypes I and II) should be strongly advised not to use artificial tanning devices, and supports the view of the WHO, which recommends that individuals should not use tanning devices if they are phototype I, have numerous naevi and/or freckles, suffered frequent sunburn in childhood, present pre-malignant or malignant skin lesions or sun-damaged skin, have applied cosmetics or take medicines which could increase their sensitivity to ultraviolet radiation.

The health authorities have an important role to play in discouraging exposure to artificial ultraviolet radiation, at least in the locations devoted to physical exercise that are under the authorities' control (swimming pools, gymnasia etc.).

In practical terms, the health authorities could:
- put a stop to advertising claiming that the use of tanning devices carries no risk and may be good for one's health, and stop the promotion of artificial tanning;
- introduce or strengthen legislation in order to ensure that tanning device operators provide accurate and adequate information to their customers;
- more strictly control the age limits at which customers can be admitted (over 18 years);
- conduct occasional inspections to ensure that eye protection is actually used and proper hygiene is maintained;
- provide specific guidance for adolescents on the dangers of artificial tanning (sun protection programme).

[1] The representative of the French National Academy of Medicine on the experts' group took a different opinion on this point. See Chapter VII.2 and Annex.

Current French legislation provides that irradiance in the UVB band of type UV-1 and UV-3 appliances must not exceed 1.5 per cent of their total UVA + UVB irradiance.
For the sake of clarity and ease of interpretation, this provision could be replaced by a reference to the tropical sun at the zenith.
The effective irradiance of a tanning device should not exceed the irradiance of the tropical sun, and the spectral distribution of its radiation should be fairly close to that of the tropical sun. The irradiance and spectral distribution should meet the specifications for type 3 UV appliances as defined in the European EN 60335-2-27 standard (1997).
The UV index of a type 3 tanning appliance is approximately 12, the equivalent of a tropical sun. If the proposed changes in IEC standard 60335-2-27 were implemented, they would allow a UV index of 24 – a level of exposure not reached naturally anywhere on earth.

Most medical and scientific bodies, learned societies and international organizations recommend avoiding exposure to artificial UV radiation. If some people choose to ignore these recommendations, however, it is advisable to set certain limits: 100 $J.m^{-2}$ E_{eff} for first exposure to UV appliances, and total annual exposure of three series of ten sessions for melano-competent subjects of phototype III (15 $kJ.m^{-2}$) and phototype IV (21 $kJ.m^{-2}$).

This does not mean that the use of UV devices presents no health risks. The formula used to calculate risk has predicted a significant risk of non-melanoma skin cancer, and some clinical trials have shown a significant increase in the risk of melanoma above ten annual exposure sessions.

Regulatory changes

The working group proposes the following changes to the regulations:
- It is recommended that the exposure time offered by sunbed timers be limited by indexing it to the total power emitted by the appliance, such that the latter cannot deliver more than 8 SED units.
- All melano-compromised subjects should be informed that under no circumstances should they be exposed to artificial UV radiation.
- The prohibition on minors should be strictly enforced.
- Following the recommendation of the WHO, the customer should be required to complete, sign and date an informed consent form before beginning any series of artificial tanning sessions. One copy of the form is for the customer, while the other must be preserved for two years by the tanning salon. This document, which must be presented at the request of inspection officers, as the latter are defined by the regulations, would provide more precise information on the use of tanning devices (see the annexed draft consent form).
- The working group suggests that only type 3 appliances be allowed under French regulations; this will simplify inspections and avoid the dangerous appliances that attempts to deregulate the industry would bring onto the market.
- Advertising and promotion of tanning devices and of the establishments making them available to the public should be prohibited.
- All claims that exposure to artificial UV radiation offers health benefits should be

prohibited.

- The power of UV tanning devices should be limited to that of a tropical sun (UV index 12, or 0.3 W/m^2 eff (weighted by the erythemal effectiveness spectrum). This proposal would align the French position with that of the Scandinavian countries, where over 35 per cent of the population uses UV appliances but people are much less exposed to the sun than in France.

3. Other UV sources designed for domestic or industrial use

Some "broad-spectrum" sources supposed to reproduce the solar spectrum, including its UV components, are currently on sale. These sources are offered for direct lighting use instead of ordinary tubes and lamps, especially for home lighting and the construction of solaria, and in the workplace. The risks which must be taken into account relate in particular to the acute and long-term ophthalmic risks, the risk of photosensitization and the risk of skin cancer.

At the request of the experts' group, Afsse commissioned the Laboratoire National d'Essais (French National Test Laboratory) to perform irradiance and spectral distribution measurements in various configurations involving "broad-spectrum" lamps and tubes for domestic or similar use. While the first results on a single model of lamps and tubes show that the UV emissions are negligible, in view of the results of tests on other lamp models it may be necessary to establish a regulatory framework on the basis of the Council Directive of 19 February 1973[2]. The regulations relating to the sale and availability to the public of certain tanning devices that use ultraviolet radiation could then be extended to all UV-emitting sources made available to the public.
When selling broad-spectrum lamps, manufacturers and distributors should therefore inform consumers of the risks of prolonged exposure to UV radiation, and clearly explain the proper practices for use of their products. In fact, it seems that most of these products are not used for their initial purpose (e.g. horticulture or industrial use). Statements that this type of lamp may have a beneficial effect on health, or even that they can be used for ordinary day-to-day lighting, should be prohibited. Their use in premises open to the public, and especially to children, or as lighting in workplaces, should consequently be prohibited.

<u>InVS recommendations</u>

To improve knowledge of the exposure of the French population to ultraviolet radiation and knowledge of the effects of such exposure on the health, the InVS working group has issued the following six recommendations.

- **Recommendation 1: Improving knowledge of environmental exposure to UV radiation**

As regards environmental exposure to ultraviolet radiation, two complementary systems

[2] Directive relating to electrical material designed for use within certain voltage limits, which requires technical measures to be taken to ensure that dangerous radiation is not produced.

exist, which must be supported and whose consistency should be encouraged: a satellite measuring system and a system based on ground-level measuring stations.
These two systems are wholly complementary: the satellite system is based on measurements and a calculation that provides a grid covering the whole country, while ground-level measurements enable the model to be validated in several atmospheric situations. Coordination of these projects should be encouraged.
Measurement of the exposure to UV radiation throughout the French territory has been conducted, but only partly exploited. This project should be encouraged in order to create an ultraviolet radiation database for the whole country and evaluate and monitor exposure by associating it with a geographical information system. This would produce a digital atlas of the distribution of exposure to UV radiation, and a major source of reliable data for evaluation of the health impact of natural UV radiation. There would also be a regional quantification of the risks to different population categories.
The convergence and complementarity of these projects with the Météo France MOCAGE model should also be systematically studied.

- **Recommendation 2: To improve knowledge of behaviour relating to natural and artificial UV radiation**

It is essential to evaluate practices relating to exposure to natural and artificial UV radiation by all age groups of the population, including children, teenagers and young adults. The current French studies do not cover the whole population, and do not focus on the teenage and young adult age groups, which have the most leisure time and are the commercial target of tanning businesses.
Studies based on existing validated questionnaires should be conducted in several regions of France to take account of the differences in distribution of phototypes, sunshine and behaviour in relation to natural and artificial UV radiation. Intermittent exposure during holidays should be evaluated, including for children. The practice of exposure to artificial UV radiation (sunbeds) should be specifically studied, by describing the financial data for this market (which have never been published), investigating practices, and endeavouring to draw up more accurate profiles of the people who frequent these centres, the history of their exposure to UV radiation, and their motives. Several current cohort studies (adults and children) have been organized to give more information about environmental and nutritional exposure. The addition of a “UV exposure knowledge” arm could be envisaged.
If these studies are repeated, the impact of prevention campaigns could be measured, and their messages adapted if necessary.

- **Recommendation 3: To improve knowledge of advertising messages in relation to exposure to UV radiation**

The social representations that support and encourage exposure to UV radiation of natural and artificial origin should be analyzed. These representations, which are strongly present in advertising messages, either directly or indirectly, are a major part of the reason for exposure to UV radiation. There are also open advertising practices aimed at the general public, networks of beauty treatment professionals, and health

professionals. These messages probably represent the majority of the information messages regarding the UV risk received by the population, and are only moderately counterbalanced by health education messages. Knowledge of these advertising campaigns, analysis of their impact on the behaviour of populations, and the conformity of the messages with legislation should be systematically pursued, as should work on knowledge of the social representations of UV exposure. This project could be included in the terms of reference of the National Health Prevention and Education Institute.

- **Recommendation 4: To improve knowledge of occupational exposure to UV radiation**

Some jobs are particularly exposed to solar or artificial UV radiation. Better characterization of occupational exposure to artificial UV radiation seems necessary. This characterization of exposure could be useful for the conduct of epidemiological studies designed to confirm and improve knowledge of the health risks of such exposure, and would allow the introduction of suitable preventive measures.

- **Recommendation 5: To coordinate actions in the field of knowledge of exposure to UV radiation: proposal for an observatory of human exposure to UV radiation**

The actions required to improve knowledge of the population's exposure to UV radiation are based on a wide variety of skills. Their introduction and development should be designed to cover different fields of UV exposure. This requires a global approach, a concerted strategy between the parties involved, and an operational structure. Such an approach could be coordinated by a body which could be called the "Human UV Radiation Exposure Observatory", and would be responsible for these actions and the production of indicators.
Such an observatory should employ metrologists familiar with the physics of UV radiation, skin cancer epidemiologists and dermatologists. It should guarantee the consistency of actions in the field, and ensure that studies of the UV risk exhaustively cover the various population categories and exposure practices.
It is not essential for this body to have an independent administrative structure: agreements between establishments could govern its operation, and InVS could handle its administrative requirements.

- **Recommendation 6: To improve knowledge of the effects of UV radiation**

Non-melanoma skin cancers (squamous-cell and basal-cell carcinoma) are not subject to epidemiological surveillance in France. Knowledge of the incidence of these cancers does not necessarily require the creation of registers. In view of the moderate severity of these carcinomas, the complexity of the health care network that identifies them and their social consequences (e.g. an inability to obtain bank loans), which suggest under-declaration, the methodology of these studies should be adapted and tested at a feasibility stage. Knowledge of the incidence of lesions indicating strong UV exposure, such as naevi, should also be obtained, primarily through feasibility studies.

The organization and repetition of population studies could enable indicators of the history of past exposure to be obtained at individual level.

Annexes to report entitled

"ULTRAVIOLET RADIATION"

CURRENT KNOWLEDGE OF EXPOSURE AND HEALTH RISKS

May 2005

ANNEX 1: Evaluation methods for cosmetic sunscreen products (extract from Afssaps report)

ANNEX 2: Spectral analysis and erythemal efficacy of three representative sources of tanning equipment

ANNEX 3: Inventory of practices in various European countries and the USA relating to UV-emitting devices

ANNEX 4: Results of technical inspections of UV tanning installations and training of teachers at beauticians' schools and colleges

ANNEX 5: Obtaining informed consent before tanning sessions

ANNEX 6: Letter from Professor Jacques Bazex

ANNEX 1: Evaluation methods for cosmetic sunscreen products (extract from Afssaps report)

The efficacy of sunscreens in protecting against the short-term effects of UV radiation can be evaluated by measuring protection factors with the aid of *in vitro* and/or *in vivo* methodologies.

As regards the long-term effects of UV radiation, there is currently no scientific proof that the use of sunscreen protects against any biological effect. The methods of evaluating the action of a sunscreen on a biological effect are indirect measurements performed with the aid of *in vitro* techniques (genome protection, inhibition of biological cell effects, and protection against photo-immunosuppression).

Protection factors

(Afssaps Sunscreen Working Group /Minute no. 2/March 2003, Minutes nos. 3 and 4/April 2003 and Minute no. 8 of 15/12/03) [10].

Preamble

The labels of sunscreen products usually include wording of the following kind: "contains UVA filters", "with UVA filters", "broad-spectrum protection", "extra-broad UVA and UVB absorption spectrum,", "100% anti-UVA/UVB/IR", "blocks short UVA rays", "30A UVA protection factor", "Reinforced UVA protection", "UVB 30/UVA 30", "25B 7 A", "SPF 30, UVA factor 10", "SPF 60, IPD 55, PPD 12", "broad spectrum according to Australian standard", etc.

These indications, which are based on different measurement methods, cause confusion among French consumers rather then providing information.

Moreover, awareness of the biological effects associated with exposure to UVA radiation has accelerated the development and marketing of sunscreens offering protection against UVA radiation [10 (1), (4), (7), (13)]. However, there is currently no standardization of the anti-UVA protection factors printed on products. This situation is due to the difficulty of defining UVA protection, and associating a standardized evaluation method with it [10 (16)]. In the field of international harmonization and standardization, the present aim is to develop a single validated *in vitro* method correlated with the *in vivo* PPD method. However, UVA labelling does not currently enable users to tell which of two products with the same sun protection factor (SPF) offers the greatest protection against UVA radiation.

Principles and aims of methods used to determine protection factors

The methods used to determine protection factors can be implemented *in vivo* or *in vitro,* but are not based on the same principles.

In vivo, measurement of the SPF (Sun Protection Factor) is based on the erythemal response to UVB radiation, while measurement of anti-UVA factors is based on Immediate Pigment Darkening (IPD) or Persistent Pigment Darkening (PPD).

In vitro, the principle of methods for determining the protective efficacy of sunscreens is based on the Beer-Lambert law, which involves measuring the absorption spectrum of the filter in solution, or of the product applied to a substrate that simulates the skin texture, by transmission spectrophotometry.
The efficacy of protection against UVB or UVA radiation or both, or their effects on a skin response, is then determined by calculating the quantity of "effective" energy that reaches the epidermis in both UVA and UVB radiation, with and without taking into account the action spectrum of UV radiation for the damage in question.

In vivo methodologies used to determine protection factors

In vivo determination of UVB protection factors

The *in vivo* method used in Europe to evaluate protection against the short-term effects of UVB radiation is the one established by COLIPA (1994) in humans [9]. 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 (MEDnp).

The advantages and limitations of the SPF *in vivo* include the following parameters:

- *Advantages:*
  - The method used to evaluate protection against the short-term effects of UVB radiation (SPF) established by COLIPA (1994), which is widely used in Europe, is currently being revised in order to harmonize and globalize the SPF.
  - Protection against solar erythema is directly evaluated.
- *Limitations:*
  - The method of evaluating protection against the short-term effects of UVB radiation (SPF) requires modifications to the methodology, especially as regards the number of subjects (the minimum should be changed to 10 and the maximum to 20), the 95% confidence interval, for which the standard deviation from the mean should be under 17%, a reduction to 12% in the doses of UV radiation for high SPFs, and redefinition of the characteristics of the solar simulator).
  - The dose used in trials (2 mg/cm^2) is approximately 3 times higher than the amount currently used by consumers.

According to the experts in the group, the UVB factor obtained by determination of the SPF (COLIPA method) should not be an average factor with a 95% confidence interval that must be under 17%, but a determination of the minimum SPF (COLIPA method) that protects 90% of users or a duly validated equivalent methodology, as proposed by the experts.

Determination of UVA protection factors [10]

⇨ *In vivo* methodologies designed to determine UVA protection factors

France is one of the few European countries to use *in vivo* methods of evaluating UVA protection factors. These methodologies are based on observation and measurement of a biological response by the skin which is specific to UVA radiation: IPD (Immediate Pigment Darkening) or PPD (Persistent Pigment Darkening). As regards the factors printed on packaging, different wording is possible, depending on the methodology used and the country from which the product originates. At present, there is no standardization of the UVA protection factors printed on products.

- *Erythema protection factor and phototoxic protection factor*

These methods are based on measurement of the erythema or pigment darkening induced, and calculation of the protection factor similar to that of the SPF. This method is rarely used nowadays, as it is unreliable. The phototoxic method required the use of psoralens, which is ethically unacceptable.

- *IPD: Immediate Pigment Darkening*

The pigment darkening induced by UVA radiation as a result of oxidation of melanin and its precursors (the Meirowski phenomenon) is measured immediately after irradiation and for 15 minutes thereafter. This skin pigment darkening, which appears shortly after exposure to UVA radiation, is temporary, partly reversible when exposure ends, and oxygen-dependent. When exposure ends, the colour fades gradually but rapidly for two hours, and then fades more slowly for 24 hours. The skin colour observed within two hours is called Immediate Pigment Darkening (IPD), and that observed subsequently is called Persistent Pigment Darkening (PPD). The wavelength which is most effective in inducing IPD is around 340 nm. The dose/response curves are linear above 4 J/cm^2 [10.(11)], [10.(12)].

An IPD protection factor is obtained by calculating the ratio between the doses required to produce the response with and without sunscreen applied to the skin, as in the case of the SPF.

- *Advantages:* the methodology is easy to use.
- *Limitations:*
  - Unrealistic UVA doses (1-6 J/cm^2).
  - Photoinstability of filters not taken into account due to low doses.
  - Measurement taken in the area in which pigment darkening fades rapidly (steep slope), causing the protection factor thus obtained to be overestimated.
  - Pigment darkening is relatively difficult to assess. As the reading is taken shortly after irradiation, pigment darkening may be mistaken for thermal erythema.
  - Uncertain reproducibility.
  - Its clinical significance is considered low by some critics, because the action spectrum of IPD is different from the action spectra of erythema, skin cancer and photoaging.
  - Only volunteers belonging to phototypes II, III and IV are included in the test.

- *PPD (Persistent Pigment Darkening)*

This method derives from IPD. The pigment darkening induced by UVA radiation is measured two hours after irradiation, i.e. when the darkening has stabilized. The calculation is performed in the same way as for IPD.

- *Advantages:*
  - The doses of UVA radiation applied (15 J/cm^2) are more realistic than for IPD, and the photoinstability of filters is taken into account.
    The measurement is taken in a stabilized area of pigment darkening, which makes the reading more reliable.
- *Limitations:*
  - The cost of the method, largely due to the fact that the volunteers are immobilized for a fairly long period, from irradiation to reading.
  - Only volunteers belonging to phototypes II, III and IV are included in the test. The problem of the action spectrum is the same as for IPD.

⇨ *In vitro* methodologies used to determine UVA protection factors

In vitro, the Sayre/Agin [10.(14)] and Diffey/Robson [10.(5)], [10.(6)] method, used since the 1990s, involves a comparative measurement, with the aid of an integrating-sphere spectroradiometer, of the transmission from 290 nm to 400 nm every 5 nm, the specimen being subjected to UVA radiation from a stable known source covering the whole of the UV spectrum (xenon not filtered).

The intensities of the UVA radiation transmitted are measured by a detector after passing through a monochromator. The monochromatic protection factor (mPF_λ) is the ratio of the UV intensities recorded at a wavelength λ before and after application of the product.
Different protection factors can be calculated from the monochromatic values obtained. The main methods of calculation and the variations on the basic method are set out in the table overleaf:

UV Protection	UVA Protection				
Erythemal UV protection (SPF)	Erythemal UVA protection	Average UVA protection factor (PF)	UVA/UVB ratio on A(λ): Boots Star Rating System	UVA/UVB ratio on mPFλ	Critical wavelength λc (concept of broad spectrum)
Estimate of *in vitro* efficacy of product against erythema induced by the entire UV spectrum	Estimate of *in vitro* efficacy of the product against erythema induced by UVA radiation (approx. 16% of UVA radiation contributes to erythema)	Arithmetical mean of monochromatic protection factors mPF (λ) calculated between 320 and 400 nm	Optical density values represented as a function of wavelength and calculation of areas by wavelength unit under the UVA and UVB portions by integration:	Monochromatic protection values (mPFλ) represented as a function of wavelength and calculation of areas by wavelength unit under the UVA and B portions by integration:	λc: wavelength for which the area under the optical density curve A(λ) integrated from 290 to λc is equal to 90% of the area integrated from 290 to 400 nm
$$SPF = \frac{\sum_{290\,nm}^{400\,NM} E(\lambda).\varepsilon(\lambda)}{\sum_{290\,nm}^{400\,NM} E(\lambda).\varepsilon(\lambda)/MFA(\lambda)}$$	$$PFAe = \frac{\sum_{320\,NM}^{400\,NM} E(\lambda).\varepsilon(\lambda)}{\sum_{320\,nm}^{400\,NM} E(\lambda).\varepsilon(\lambda)/MFA(\lambda)}$$	$$PFAm = \frac{\sum_{320\,NM}^{400\,NM} MFA(\lambda).\Delta(\lambda)}{\sum_{320\,nm}^{400\,NM} \Delta(\lambda)}$$	$$UVA/UVB(A_\lambda) = \frac{\int_{320\,NM}^{400\,NM} A(\lambda).D\lambda. / \int_{320\,NM}^{400\,NM} D\lambda.}{\int_{290\,NM}^{320\,NM} A(\lambda) ./ \int_{290\,NM}^{320\,NM} D\lambda.}$$	$$UVA/UVB(mPF\lambda) = \frac{\int_{320\,NM}^{400\,NM} MFA(\lambda).D\lambda. / \int_{320\,NM}^{400\,NM} D\lambda.}{\int_{290\,NM}^{320\,NM} MFA(\lambda) ./ \int_{290\,NM}^{320\,NM} D\lambda.}$$	**λC SUCH THAT:** $$\int_{290\,NM}^{\lambda CNM} A(\lambda).D\lambda = 0.9 \int_{290\,NM}^{400\,NM} A(\lambda).D\lambda$$
SPF = Erythemal UV protection factor E(λ) = Solar spectral irradiation at ground level ε(λ) = Erythemal action spectrum (CIE 1987) mFA(λ) determined, for example, every 5 nm between 290 and 400 nm	PFAe = Erythemal UVA protection factor E(λ) = Solar spectral irradiation at ground level ε(λ) = Erythemal action spectrum (CIE 1987) mFA(λ) determined, for example, every 5 nm between 320 and 400 nm	Δ(λ) = Wavelength interval chosen, e.g. 5 nm	A(λ) = Optical density associated with transmittance T(λ) and mFAλ of product: OD = A(λ) = -log [T(λ)] = log[mFA(λ)]		This method is intended to express the breadth of the absorption spectrum of the product throughout the UV domain, especially its extent in UVA
Quality of solar spectral irradiation taken into account: necessary standardization of spectrum used; E(λ) = intensity of terrestrial spectral radiation of sun at midday at the latitude of 40°N, with an angle of 20° from the zenith and an ozone layer of 0.305 nm			This ratio varies from 0 to 1. It is used to classify products into 5 categories (stars)		
Advantages: Speed, simplicity, low cost, easy implementation, repeatability					
- Integration of the whole spectrum - Methodology recognized for performance of intra-laboratory screening tests	- Methodology recognized for performance of intra-laboratory screening tests			Associated with the monochromatic protection factor, and represents the real attenuation of UV radiation by the product at each wavelength	Not strongly dependent on product application conditions, as it does not give any information about the amplitude of attenuation, but its breadth
Disadvantages					
- Not validated by COLIPA due to poor inter-laboratory reproducibility - Limitations: support effect, certain filters, certain formulations, certain factors	- Limitations: support effect, certain filters, certain formulations, certain factors	Expression of results/ protection level	Varying the ratio at UVB level is sufficient to obtain good UVA protection		- Expression of results/level of protection (the law of all or nothing). - Does not take account of long UVA. The law of all or nothing:

- *Australian standard AS/NZS 2604, 1997*

The official Australian method (AS/NZS-2604, 1993, revised in 1997 and 1998) involves determining the transmission values of products tested between 320 and 360 nm. The products must block at least 90% of UVA radiation out of the whole range defined. Four methods are proposed: the first two, conducted in a quartz cell, measure the percentage transmission of the product in solution in a solvent mixture, while the last two measure the transmission of the product applied to quartz plates.

If over 90% of the radiation is blocked, the product conforms to the Australian standard. This method is not very representative of real conditions, but offers good reproducibility. It takes little account of long UVA radiation (UVA1) [10.(17)].

- *APP Method / UVA-Protection Percentage*

A similar methodology, but a different method of calculation.

- *Boots star rating system*

Boots is the market leader for sunscreens in the UK. The company has developed and implemented a UVA protection labelling system. The UVA protection is indicated by stars: one star corresponds to “moderate”, and four stars to “maximum”. The system is based on measurement of optical density values represented as a function of wavelength, and calculation of the areas per wavelength unit under the UVA and UVB portions, by integration, of a specimen applied to a substrate that simulates the porosity and texture of the skin.

The result is evaluated by calculating the ratio of total absorption in the UVA spectrum to total absorption in the UVB spectrum, called the UVA ratio. However, this method is not representative of real conditions.

- *Critical wavelength method*

The critical wavelength method evaluates the uniformity of the absorption spectrum of a sunscreen. The critical wavelength is the wavelength from which the integral of the absorption spectrum curve reaches 90% of the integral between 290 and 400 nm. 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”. This method is often considered to be insufficiently discriminating.

⇨ Choice of method used to determine UVA protection factors

The reviews of methods presented in the literature do not give a clear-cut opinion of a particular methodology [10(10)], [10(12)], but depend on which biological or radiation effects the authors are interested in, and the action spectrum they focus on.

A combination of *in vivo* and *in vitro* methods is often considered to provide the most reliable evaluation of UVA protection.

The PPD method seems to be the most popular *in vivo* method today, although some

authors consider that its significance is insufficient (action spectrum mainly active around 340-360 nm). This method has formed the subject of numerous validations, especially by French manufacturers' teams, whose conclusions indicate that it is sufficiently precise and reliable.

Some publications show that PPD allows the levels of protection against UVA-induced cell damage to be quantified.

The PPD method has been tested and accepted by the Japanese Association of Cosmetic Manufacturers as the official UVA evaluation and labelling method for sunscreen products in Japan since 1 January 1996 [10. (8)]. This is the *in vivo* method most commonly used, but manufacturers are working on the development of *in vitro* methods correlated with PPD.

⇨ Conclusion

Despite its weaknesses, the PPD method currently appears to be the most interesting of the various approaches proposed to evaluate UVA protection. The method proposed by the DGK (German Society for Scientific and Applied Cosmetics), with which encouraging results have been obtained, is also worthy of attention. The new methods under development and their correlation with existing methods, especially PPD, should also be taken into consideration in future

Summary of methods of measuring sun protection factors that protect against the short-term effects of UV radiation:

Parameter measured	Methodology	Recognition of method	Reliability
ANTI-UVB FACTORS			
Appraisal of erythema	*In vivo* in humans	COLIPA method widely used in Europe. Undergoing harmonization with a view to world recognition.	The new version should finalize the standardization of the method, which is still open to criticism
Transmission spectrophotometry	*In vitro:* based on the Beer-Lambert law		
ANTI-UVA FACTORS			
Photo-oxidative methods - Persistent Pigment Darkening measurements: (reading after 2h) = PPD (immediate reading) = IPD	*In vivo* in humans	No international validation	Bias (phototypes III and IV)
Transmission spectrophotometry	*In vitro:* based on the Beer-Lambert law	Under development at European level	Needs standardization due to variations: - Diffey method - modified Diffey method (Australian standard) - modified Diffey method

			(Boots method)

The description of the methodologies used to measure protection factors gives rise to the following comments:

- no opposition between the *in vitro* (physical) and *in vivo* (biological) approaches
- complementarity of *in vitro* and *in vivo* methods (screening and photostability *in vitro*, biological effects *in vivo*)
- correlations between *in vivo/in vitro* methods currently not well established, and criticized.

⇨ *In vitro*, the advantages and limitations of the tests include the following parameters:

- *Advantages:*
  - UVA protection measurements (UVA/UVB ratio, broad spectrum, UVA protection factor, etc.).
  - Repeatability and reproducibility (in particular allowing the implementation of photostability studies).
  - Simple, rapid, non-onerous methods allowing multiple controls for comparison purposes and for quality control of products.

- *Limitations:*
  - No reference standards.
  - Measurement substrate: should be transparent to UV radiation, non-fluorescent, photostable, compatible with the formulation, allowing even spreading (pigskin, human epidermis or *stratum corneum*, rough silica plate, adhesive film such as Transpore™, polymethyl methacrylate (PMMA) plates.
  - Physical and optical limits of measuring apparatus (the quantities applied *in vitro* must be consistent with the physical limit of the apparatus.
  - Quantity of product applied and spreading technique (obtaining a better correlation with the SPF *in vivo* while reducing the quantity applied to 0.75 mg/cm^2.
  - Lack of harmonization of *in vitro* methodologies for determining sun protection. The main difficulty involved is the expression of the results in terms of a sun protection level. In fact, while these methods are quantifiable, there is no extrapolation in terms of sun protection.
  - No evaluation on irradiated products.

⇨ *In vivo*, as regards UVA protection factors, the following parameters are among the advantages and limitations of the tests:

- *Advantages:*
  - The method used to evaluate protection against the short-term effects of UVA radiation (PPD), which is standardized, has been recognized by Japan since 1996 and used by many manufacturers [10. (8)].
- *Limitations:*
  - No international harmonization of the UVA protection factors displayed on products.

- PPD attracts criticism, especially due to the use of volunteers with phototypes III and IV. The question arises as to why PPD is chosen as a measurement parameter: for ethical (good marker for UVA erythema), physiological, financial or technological reasons?
- The experts query the significance of the UVA protection factors displayed on products, which are sometimes very high.
  The present objective is to develop a single validated *in vitro* method correlated with the *in vivo* PPD method.

Methods used to evaluate the protection provided by sunscreens against photo-induced aging

At present, there is no validated method of evaluating photo-induced aging.

In vivo studies have been conducted on animals, especially hairless mice, to evaluate the dermal elastosis induced by UVB radiation after repeated irradiations.

Modelling tests to evaluate elastosis have also been conducted, using mouse lines transfected by a human elastin-coding gene.
Few *in vivo* clinical trials on photoprotection and skin aging have been conducted in humans. The trials conducted were placebo-controlled, and relate to skin biopsies photo-exposed after application of a sunscreen.

Methods used to evaluate the protection provided by sunscreens against UV-induced immunosuppression [4]

Evaluation methods relating to photoimmunosuppression (PIS) and photoprotection are based on different experimental models in animals and humans (hairless and haired mice, tissue explants, and healthy volunteers), and depend on the type of immune reaction evaluated (*in vitro* antigen-presenting activity by performing mixed lymphocyte or lymphoepidermal cultures, and stages of induction or detection of contact hypersensitivity (CH) reactions and delayed type hypersensitivity (DTH) reactions).

Studies conducted on humans only evaluate protection against certain types of immune reaction which are modified by UV radiation: stages of induction and detection of CH reactions, DTH reactions, number and antigen-presenting activity of LCs, and production of cytokines.

In vivo, hypersensitivity reactions are used in animals and humans to evaluate photoimmunological effects. The study models enabling PIS to be evaluated are as follows:

- contact hypersensitivity reactions (CHR)
- delayed type hypersensitivity reactions (DTHR)
- allogenic presentation

- production of cytokines (interleukins, etc.).

Contact hypersensitivity reactions (CHR), and especially the stages of sensitization and detection, serve as models for *in vivo* evaluation of the immunosuppressive action of UV radiation. Inability to sensitize an individual after application of hapten to irradiated skin defines the concept of photo-induced skin tolerance. Applied to tumour neo-antigens, this acquired tolerance demonstrates the role of PIS in promoting epithelial cells that are liable to become cancerous.

It is often difficult to draw up experimental protocols relating to the induction phase, as it requires the use of sensitizing agents (which are often irritants) and the formation of different groups of healthy volunteers. The intensity of photoimmunological effects depends on the doses of UV radiation delivered, and whether the irradiation is acute or chronic.

The implementation of experimental protocols relating to the detection stage is easier, as each subject known to be allergic can act as his/her own control.

Delayed type hypersensitivity reactions (DTHR) to bacterial or fungal antigens affected by exposure to UV radiation have recently served as study models for evaluation of various sun filters against PIS.

At present, there are no immunosuppression markers, bioassays or validated experimental models which enable PIS to be evaluated.
It is consequently impossible to define an immunosuppression protection factor (IPF) and establish a correlation between protection against the inflammatory skin reaction as defined by the SPF and protection against alterations of skin immunity induced *in vivo* by solar exposure.

The few studies that have endeavoured to compare IPF and SPF have given contradictory results, in which the IPFs are higher or lower than the SPFs. In view of the diversity of the experimental conditions and the difficulty of transposing the results from mice to humans, it is currently impossible to compare the SPF and IPF. However, immunosuppression probably appears at a lower dose than that required to produce an erythematous reaction.

Methods used to evaluate sunscreens in the prevention of photodermatitis

These methods are mainly usage tests, conducted under natural, spontaneous conditions of exposure to sun under medical supervision (e.g. observation of polymorphous light eruptions triggered by application of a product to a skin area/control area).

Pursuant to the Huriet Act, they also include laboratory challenge tests designed to trigger photodermatitis by planned exposure to UV radiation. These tests are often conducted on patients who suffer from polymorphous light eruptions; 30 seconds' exposure at 0.5 J/cm^2 can be enough to trigger polymorphous light eruptions in some

patients. UVA sunscreens with a very high protection factor are required for this type of patient.

Methods of evaluating photogenotoxicity

(Afssaps Sunscreen Working Group /Minute no. 4/April 2003) [11].

There is currently no validated method allowing *in vivo* evaluation of the protection provided by sun filters against the long-term effects of UV radiation, especially on the DNA. The protection provided by sunscreens against the appearance of skin cancer is usually evaluated *in vitro* and *in vivo* with animal models.

DNA protection is evaluated indirectly with the aid of several markers, including:

1) Testing for DNA photoproducts such as 8-oxoguanine or pyrimidine dimers (comet test, immunohistochemical analysis, etc.).

2) Evidence of DNA repair (comet test, UDS test, etc.).

3) Monitoring of apoptosis (measurement of sunburn cells by histology, etc.).

4) Induction of p53 (immunohistochemical analysis, etc.).
   In vitro, sunscreens reduce the appearance of mutations of the p53 gene, a suppressor gene that plays an important role in regulating the cell cycle and cell apoptosis, in epidermal cells. P53 can be found in the skin of irradiated mice months before skin tumours develop. It is therefore an essential early factor in photocarcinogenesis.

   However, studies relating to the protection of gene p53 against mutations are difficult to interpret, and cannot be considered a predictive test as they stand. Account must be taken of the fact that the function of p53 is to allow a cell to repair its DNA damage and to commence apoptosis. Apoptosis is a crucial mechanism for eliminating cells undergoing mutation, and therefore avoiding carcinogenesis; protecting against induction of p53 is therefore a double-edged sword.

In animals, the application of sunscreens partly reduces the induction of tumour progression by exposure to UVB radiation and the formation of sunburn cells. However, these results seem to depend on the type of animal, the UV radiation used, and the sun filter.
Some studies conducted on animals have demonstrated certain beneficial effects of sun filters on the induction of photo-induced tumours, but there are few of these studies, which were conducted under conditions that are difficult to compare, and are not currently predictive of the effects on humans.

The currently available data, obtained *in vitro* and *in vivo* in animals, tends to demonstrate that sun filters may have a beneficial effect against the adverse long-term

effects of solar exposure. However, a number of questions still remain, such as the extent of the protective effects, the exact proportion of the anti-UVB and anti-UVA effects, the erythemal protection factor value as from which protection against effects on the DNA can be expected, and the most significant biological marker to monitor.

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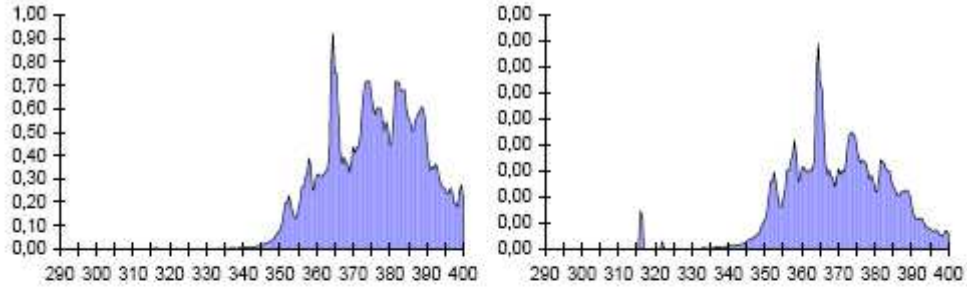
ANNEX 2: Spectral analysis and erythemal efficacy of three representative sources of tanning equipment

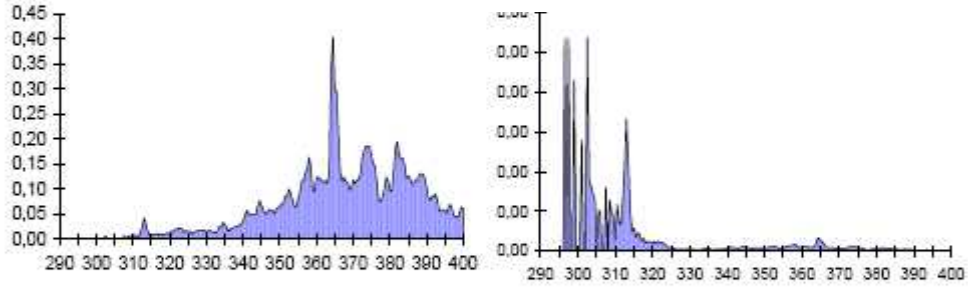
Spectral analysis and erythemal efficacy of three representative sources of tanning equipment

Spectral emission of sources (spectral analysis)		**Erythemal efficacy** (Weighting by erythemal efficacy spectrum)

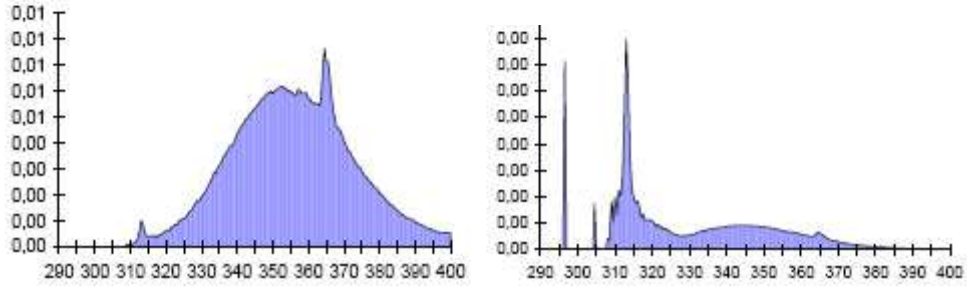
UVASUN 5000 : CEI Type I



FILTERED MERCURY LAMP (PHILIPS HB 411): CEI type III)



FLUORESCENT TUBE TL 09 (Philips HB 311): CEI Type III



ANNEX 3: Inventory of practices in various European countries and the USA relating to UV-emitting devices

Inventory of practices in various European countries and the USA

Country	UV Type 60335-2-27	Sale to Public	Declaration	Technical inspection	Qualified personnel present	Personnel training	Mandatory warnings	Minimum age
Belgium	UV-3	—	?	—	—	—	Yes	18
Canada	No	—	No	No	No	—	Yes	16
Spain	UV-3	—	Yes	Yes 1 year	Yes	Yes	Yes	18
Finland	UV-3	—	No	—	Yes	—	Yes	18
France	UV-1 UV-3 UVB < 1.5% total UV	UV-3	Yes	Yes 2 years	Yes	Yes	Yes	18
Norway	UV-3	—	Yes import	No	—	—	Yes	—
Sweden	UV-3	UV-3	Yes	No	Yes	—	Yes	18
USA	No	—	—	—	—	—	Yes	—

Country	Exclusion of phototype	Medic.	Consent form	Obligation to wear glasses*	Cosmetics removed	1st session ($J.m^{-2}$)	Annual total $kJ.m^{-2}$	UVC $W.m^{-2}$	Timer	Danger signs
Belgium	I	—	Yes	Yes	—	½ session	—	—	—	—
Canada	—	No	—	Yes	—	—	—	<0.003	—	Yes
Spain	I	Yes	Yes + card	Yes	Yes	100	—	0.00	—	—
Finland	—	—		Yes	—	100	5	—	—	—
France	I	Yes	No	Yes	Yes	100	15	—	30 min 1 h	—
Norway	—	Yes	—	Yes	—	100	—	<0.002	—	—
Sweden	—	—	—	Yes	—	100	—	—	30 min	—
USA	—	—	—	Yes	—	117	412 MED**	—	4 MED	—

* = conform to EN170 CE marking UVB < 0.001, UVA < 0.01

** = MED = 200 $J.m^{-2}$ erythemal eff.

ANNEX 4: Results of technical inspections of UV tanning installations and training of teachers at beauticians' schools and colleges

Results of technical inspections

Year	Number	Conformity	Minor non-confs.	Major non-confs.	No declaration	No doc'n	Unqual. personnel
1999	2681	1424 (51%)	880 (33%)	473 (18%)			
2000	2708	1488 (55%)	1285 (47%)	459 (18%)			
2001	2641	1937 (73%)	611 (23%)	285 (11%)	121	105	66
2002	1408	941 (67%)	336 (24%)	254 (18%)	156 (11%)	46 (3%)	20 (1%)
2003	1330	955 (72%)	285 (21%)	200 (15%)	114 (9%)	112 (8%)	28 (2%)
TOTAL	**8060**						
Periodic inspections							
2002	2063	1746 (85%)	286 (14%)	152 (7%)		46 (2%)	20 (1%)
2003	2405	1950 (81%)	321 (13%)	194 (8%)	67 (3%)	58 (2%)	49 (2%)
TOTAL	**4468**						

Declarations made to Prefects (DDCCRF [Departmental Authority for Competition, Consumer Affairs and Fraud Control] or DDASS [Departmental Authority for Health and Social Affairs])

Inventory (ordered in 2004) of the number of UV tanning installations declared since the decree came into force:

- **12,000** UV tanning installations have been declared, 8,368 of which are beauty parlours
- **13,678 UV devices** are held, **1,218** of which are **type UV-1 and 11,312** of which are **type UV-3.** 1,145 devices of "undetermined" type are listed in the inventory.

Sixty-four French departmental authorities performed inspections in 2004, which revealed that 317 businesses had closed down, bringing the probable number of installations to 11,728.

DGCCRF inspections

The DGCCRF (Authority for Competition, Consumer Affairs and Fraud Control) performed a number of inspections and surveys between 2000 and 2003:

DGCCRF inspections and surveys

Date (Departmental Authorities)	Number of establishments inspected	Reports	Order to conform
2000 (66)	1666	91	440
2002 (57)	1478	106	287
Q3 2003 (21)	555	111	168

In an information note issued in 2004, the DGCCRF reported as follows:

- beauty professionals are well informed about the regulations; non-conformities were mainly found in the hotel trade
- the declaration obligation was met on the whole

- technical inspections found a 37% contravention rate (major and minor non-conformities)
- in most establishments, at least one person holds the required qualification, but the need for refresher courses (every 5 years) is not clearly perceived
- information aimed at the public is generally well provided, but information about undesirable risks is often absent
- protective glasses with CE markings are generally provided.

In conclusion, the regulations are unevenly applied, but the follow-up of orders to conform shows that the rate of conformity is high after a DGCCRF inspection. "The last survey confirms the improvement in the safety of UV devices in the beauty sectors… The difficulties of the approved organizations, which are reliant on a small number of measuring devices and a small number of authorized, trained inspectors… The setting up… of numerous tanning centres has led to the disappearance… or termination of this service by beauticians … Inspections should be continued and strenghtened in tanning centres … sports and fitness centres, whose managers appear to be less aware of the dangers of UV radiation than beauty professionals". If the number of initial inspections performed since 1998 by the approved technical inspection bodies is compared with the number of establishments declared to DDASSs and DDCCRFs, the deficit is around 25%. The total number of establishments supplying UV radiation to the public is therefore likely to be around 12,000 at most in France. This figure is very different from the 40,000 devices claimed by some supposedly "representative members of the profession". The difference between establishments/devices declared and inspected is due to installations in hotels and service apartments, which are not inspected by the DGCCRF or technical inspection bodies.

Teaching of UV training: teacher training

Teacher training (situation at end of 2004)

Number of teacher training sessions	**11**	
Number of diplomas awarded	580	
Number of teachers trained	550	
Of which State education		180
Number of refresher sessions	3	
Number of teachers who have attended refresher courses	198	

Date of initial training	Number of initial training courses	Year of refresher course	Number of refresher courses
02/12/1997	69	12/2002	37
21/01/1998	80	01/2003	44
07/04/1998	66	01/2003	42
19/11/1998	34	01/2003 – (2004)	11
17/12/1998	39	01/2003 – (2004)	8
	sub-total 288		**sub-total 142**
08/04/1999	31	(2004)	0
03/02/2000	34	2003 – (2005)	2
12/04/2001	41	2003 – (2006)	1
31/01/2002	58	(2007)	
16/01/2003	61	(2008)	
22/01/2004	67	(2009)	
TOTAL	**580**		**198**

NB: the number of vocational training courses held subsequently by trained teachers in their associated establishments is unknown.

ANNEX 5: Obtaining informed consent before a series of tanning sessions

This project was launched by the WHO in its document "Artificial tanning: risks and recommendations". This document is intended by the WHO to make clients aware of the dangers of UV radiation, dissuade them from undergoing multiple exposures to both artificial UV and solar radiation (surveys show that consumers of artificial UV radiation are also sunbathing "addicts"), and draw particular attention to the prohibition on UV sessions for minors. Isolated projects have already been conducted in France since Decree 97-617 came into force (Saône et Loire DDASS).

This document has been criticized in some quarters on the ground that it reduces the liability of professionals. Other criticisms, similar to those made during the passing of decree no. 97-617, have been raised. According to some critics, the French health authorities are rendered legally liable by the mere passing of legislation regarding the use of a known carcinogen, because UV radiation must be considered risk-free as it forms the subject of legislation by the public authorities. However, the same could be said of other known carcinogenic products, such as tobacco and alcohol, which also benefit from a legislative and regulatory framework. The working group considers that this document would have dissuasive effects and encourage clients to take responsibility, which would outweigh the possible unfavourable effects.

Example of client's consent form: important information relating to the use of sunbeds

Please read the following information carefully.

Exposure to ultraviolet (UV) radiation leads to skin aging and can cause skin cancer.

People who have fair skin or do not tan easily should not use sunbeds.

All intentional exposure to artificial UV radiation must be avoided during the 48 hours before and after exposure to sunlight or a sunbed.

Protective sunglasses must be worn during exposure to artificial UV radiation. You must not read during a tanning session.

The risk is higher, and the use of sunbeds is inadvisable, if:

- you have already been treated at least once for solar keratosis or skin cancer; or
- you have already presented an abnormal reaction or allergy to light.

The risk may be higher if you are pregnant, if you take certain medicines, or if you apply medicines or certain cosmetics to your skin.

In case of doubt, please consult your doctor before undergoing a UV radiation session.

I, the undersigned (name in block capitals) ……., aged over 18 years, have carefully read and fully understood the above information and decided to undergo exposure to UV radiation in this establishment.

Signature:

Date:

Name of establishment:

ANNEX 6: Letter from Professor Jacques Bazex

Toulouse Hospital

Toulouse, 3 May 2005

To: Dr. Gilles Dixsaut,
Inspector-General of Public Health
Head of Physical Agents Unit
French Environmental Health Safety Agency
27-31 Avenue du Général Leclerc
94704 Maisons-Alfort Cedex

VE/JB

Dear Sir,

I should be grateful if you would send me a copy of the final draft drawn up by our working group.

I would remind you of the two points under discussion.

Firstly, it seems wholly unacceptable for the slightest medical judgment to be left to a person who operates sunbeds. This person cannot be considered capable of assessing skin type, questioning the client about tolerance of exposure to the sun, judging the nature of a pigmented element, knowing whether patients are taking medicines, etc.; these are things which should be done by a member of the medical profession.

The second point relates to the concept of tolerating an activity while controlling it. I believe it is perfectly possible to pass legislation concerning the devices which can be distributed and indicating their characteristics, but I do not think it is acceptable to say that a certain device can be used for tanning purposes.

As I have already said, this would give the practice a certain scientific and medical backing.

If it is impossible to prohibit this practice, it should be borne in mind that among the activities regulated by the State, protection of the health of individuals is one of the primary concerns, and the principle of prevention is imperative.

I should be very pleased if we could discuss these matters again.

Yours faithfully,

Prof. Jacques Bazex