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Fall from GRASE: The Sunsetting of the Sunscreen Innovation Act

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ABSTRACT

The 2020 Coronavirus Aid, Relief, and Economic Security (CARES) Act terminated the Sunscreen Innovation Act (SIA) that the Food & Drug Administration (FDA) uses to determine sunscreen actives as safe and effective for human use. The Act also nullified a recent FDA proposal that reclassified 14 organic sunscreen actives as either not safe for human use or requires more data before being used in humans. Most sunscreen actives were approved in 1978; since that time the FDA has determined that over the last 20 years several changes have occurred leading to a substantial increase in sunscreen usage and exposure that increases the potential health risks associated with their use. Based on the scientific literature for the actives reviewed, it is clear that the SIA is needed to assure that sunscreen and other over-the-counter drugs are safe and efficacious for human use prior to entering the marketplace.

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On March 27, 2020 Bill H.R. 748 known as the "Coronavirus Aid, Relief, and Economic Security Act" or the "CARES Act" became Public Law No: 116-136 (Congress.gov 2020). Included on page 159 is "Section 586.SUNSET" which removes, without replacing, on September 30, 2022 the Sunscreen Innovation Act (SIA) which is used by the Food & Drug Administration (FDA) to request specific information such as toxicokinetics, carcinogenicity, reproductive toxicity, pediatric considerations and alike to determine if a Over-The-Counter (OTC) sunscreen drug active ingredient is Generally Recognized As Safe & Effective (GRASE) for human use (FDA 2016a). The SIA also requires FDA to establish timeframes for review of OTC drugs other than sunscreen active ingredients (FDA 2016b).

FDA published in the February 26, 2019 Federal Register a notice removing 14 organic sunscreen actives from the GRASE list "Because the public record does not currently contain sufficient data to support positive GRASE determinations" (FDA 2019). FDA further explains: "For example, the available literature includes studies indicating that oxybenzone is absorbed through the skin to a greater extent than previously understood and can lead to significant systemic exposure, as well as data showing the presence of oxybenzone in human breast milk, amniotic fluid, urine, and blood plasma. The significant systemic availability of oxybenzone, coupled with a lack of data evaluating the full extent of its absorption potential, is a concern, among other reasons, because of questions raised in the published literature regarding the potential for endocrine activity in connection with systemic oxybenzone exposure. Nearly all of these sunscreen active ingredients also have limited or no data characterizing their absorption." To further demonstrate their concerns, FDA published two studies (Matta 2019, Matta 2020) demonstrating that avobenzone, oxybenzone, octocrylene, homosalate, octisalate, octinoxate and ecamsule absorbed through the skin above the Level Of Concern (LOC) for systemic toxicity (0.5ng/ml). "FDA has provided guidance that sunscreen active ingredients with systemic absorption greater than 0.5 ng/mL or with safety concerns should undergo nonclinical toxicology assessment including systemic carcinogenicity and additional developmental and reproductive studies" (Matta 2019).

PABA and Trolamine Salicylate:

FDA stated in the Federal Register (FDA 2019) that these actives would be moved from Category I (GRASE) to Category II (Not GRASE) - "Our evaluation of the available safety data for aminobenzoic acid (PABA) and trolamine salicylate, however, has caused us to conclude that the risks associated with use of these active ingredients in sunscreen products outweigh their benefits. In the case of trolamine salicylate, these risks include the potential for serious detrimental health effects (including bleeding) caused by the anti-coagulation effects of salicylic acid and increased risk of salicylate toxicity when this ingredient is used in sunscreens. For PABA, the risks include significant rates of allergic and photoallergic skin reactions, as well as cross-sensitization with structurally similar compounds."

Oxybenzone* (CAS# 131-57-7; Molecular Weight (MW) 228.2 Dalton's)*:

Contact Dermatitis: Numerous reports of contact allergy, photoallergy, contact urticaria and, to a lesser degree, contact mediated anaphylaxis reactions in humans to oxybenzone have been reported (DiNardo and Downs 2018). In a European Commission (2006) opinion on oxybenzone, a total of 159 positive reactions were noted, leading to the conclusion that oxybenzone is a photoallergen. By way of comparison, only 19 photoallergic reactions were noted in this review to PABA. Additionally, the American Contact Dermatitis Society (Heurung 2014) observed that oxybenzone showed high rates of cross-reactivity with octocrylene and ketoprofen, both benzophenone structures. Therefore, the FDA opinion, noted above, relating to sensitization risks to PABA should also apply. Note: All of the actives discussed below have

some contact and photo-contact allergy activity, but to a lesser degree than oxybenzone.

Human Absorption: Matta (2020) observed maximum oxybenzone levels of 258.1 ng/ml or 516.2 times above the LOC for systemic toxicity in the blood after 4 applications/day for 4 days in humans. This dose represents the recommended dose for a sunscreen that one would use for 4 days at the beach. Additionally, oxybenzone persisted in the blood at levels well above the LOC after the study terminated on day 21.

Pediatric Concerns: The Swedish Research Council (EurekAlert 2006) has determined that "Children under the age of two years have not fully developed the enzymes that are believed to break down oxybenzone. This suggests, in theory, that small children will not be able to get rid of the substance as easily as adults."

Reproductive/Endocrine Disrupting Concerns: Oxybenzone and its metabolite 4-hydroxybenzophenone have been shown to negatively impact testosterone levels as well as mimic the effect of progesterone on Ca^{2+} signaling in human sperm cells, an effect that might impair human fertilization (Buck Louis 2014, Rehfeld 2016).

FDA and the National Toxicology Program (NTP) jointly reported that spermatocyte development was impaired in testes of male rat offspring and follicular development was delayed in female rats (Nakamura 2015). The scientists concluded that "exposure to less than 10,000 ppm oxybenzone does not appear to be associated with adverse effects on the reproductive system." Unfortunately, oxybenzone is commonly used in sunscreens at 60,000 parts per million (ppm) or 6%. A similar issue occurred in another report whereby oxybenzone negatively impacted gene expression profiles of the prostate and testis of male rats (Nakamura 2018). The highest dose tested was 30,000 ppm or half the typical human dose.

Hirschsprung's Disease (HSCR): Huo (2016) investigated urinary oxybenzone levels and the incidence of HSCR in 423 Chinese patients; mothers with high levels of oxybenzone had neonates that required surgical intervention for HSCR. Additionally, Huo conducted in vitro research demonstrating that oxybenzone caused abnormal migration of specific neural crest cells - a known mechanism of action for HSCR. DiNardo and Downs (2019) further demonstrated that under normal use conditions enough oxybenzone is available to the fetus during critical embryonic development to inhibit the migration of these neural crest cells.

Carcinogenicity Concerns: Oxybenzone was found to produce a marginal increase of neoplasms and an increase in nonneoplastic lesions of the testis in male rats and of the uterus and adrenal cortex in female rats along with increases in the incidences of nonneoplastic lesions of the bone marrow, spleen, kidney and liver in mice when tested at 10,000 ppm or 1% (NTP 2020). Again, oxybenzone is commonly used at six times the dose tested.

Octocrylene (CAS# 6197-30-4; MW 361.5 Dalton's):

Human Absorption: A maximum octocrylene level of 7.8 ng/mL (15.6 times LOC) was observed in the blood; unsafe levels persisted until day 10 (Matta 2020).

Carcinogenicity Concerns: Octocrylene was thought to contained low levels of an impurity called benzophenone (CAS#119-61-9; MW 182.2 Dalton's). NTP identified benzophenone as a carcinogen (Rhodes 2007), which lead to FDA banning its use as a food additive (FDA 2018), California Proposition 65 (2012) identified it as "causing cancer" and the International Agency for Research on Cancer (2013) classifies it as "possibly carcinogenic to humans - Group 2B". Furthermore, Downs et al (2020) demonstrated that levels of benzophenone observed in octocrylene were not just associated with contamination, but octocrylene's degradation via hydrolysis, which increased over time with aging. Of the 16-samples tested, benzophenone content for unaged samples was 6.3 – 185.5 ppm and for aged samples was 9.8 to 434.9 ppm. Comparing these values to the level FDA used to ban benzophenone in foods (FDA

2018) and to the standard established for the "safe level of use in foods" set by the European Food Safety Authority (EFSA) in 2017, the lowest level observed for samples was 98 times the FDA and 7 times the EFSA levels and the highest level determined for samples was 6,765 times and 507 times the FDA and EFSA levels, respectively (Table 1). Additionally, since parents tend to over apply young children with sunscreen, the pediatric considerations associated with these findings demonstrates that benzophenone exposure for 2 Kg or 10 Kg children is hundreds to thousands of times the FDA and ESFA banned/safe levels (Table 2).

Note: 70% of benzophenone can absorb through skin from topical preparations (Bronaugh 1990) and stimulates caspase 3, which is involved in photosensitization (Amar 2015) and melanoma tumor cell growth (Donato 2014).

Homosalate (CAS# 118-56-9; MW 262.4 Dalton's):

Human Absorption: A maximum homosalate level of 23.1 ng/mL (46.2 times LOC) was observed in the blood; unsafe levels persisted after the study terminated on day 21 (Matta 2020).

Carcinogenicity Concerns: European Chemicals Agency (ECHA) reports, a two-year rat feeding study was conducted on homosalate and under the test conditions, growth retardation and bone lesions were observed at 1.0 and 2.0% and gross pituitary lesions at 0.5% methyl salicylate (expressed as homosalate) in the diet (ECHA 1963a).

Homosalate can interact with DNA causing damage in human lymphocytes and demonstrates cytotoxic and genotoxic effects in human MCF-7 breast cancer cells (Yazar 2020). Increased motility of oestrogen-responsive MCF-7 cells were also observed after long-term exposure (>20 weeks) to homosalate with increase migration and invasion of human breast cancer cells (Alamer 2018).

Note: Alamer 2018 observed similar findings for oxybenzone and its metabolite benzophenone-1 as well as for octinoxate.

Reproductive/Endocrine Disruption Concerns: Homosalate demonstrated anti-androgenic activity in vitro in addition to estrogenic activity in human breast carcinoma cell line MDA-kb2 (Ma 2003, Jiménez-Díaz 2013); demonstrated estrogenic effects that were found to be antagonistic toward androgen and progesterone receptors (Schreurs 2005); and adversely affected the survival, proliferation, and invasiveness of human trophoblast cells causing Yang (2018) to suggest that pregnant women practice caution while using personal care products containing the ingredient.

Effects on Human Semen/Sperm: Homosalate and octisalate induced acrosome reactions similar to progesterone; "human exposure to these chemical UV filters may impair fertility by interfering with sperm function" (Rehfeld 2018). Homosalate "interferes with various sperm functions and, thereby, might impair human fertilization" (Schiffer 2014).

Note: Homosalate and octisalate are salicylate-based compounds like aspirin and salicylic acid, which are linked to two major teratogenic metabolites, 2,3-dihydroxybenzoic acid and 2,5-dihydroxybenzoic acid - Figure 1 (Karabulut 2000). Therefore, toxicokinetics and reproductive toxicology should be a major concern since they can be use in combination in a product up to 20%. Additionally, salicylate levels in a sunscreen product may be higher if a product contains butyloctyl salicylate as an inactive ingredient to boost efficacy. Similar concerns as noted by FDA for trolamine salicylate might also apply.

Octisalate (CAS# 118-60-5; MW 250.3 Dalton's):

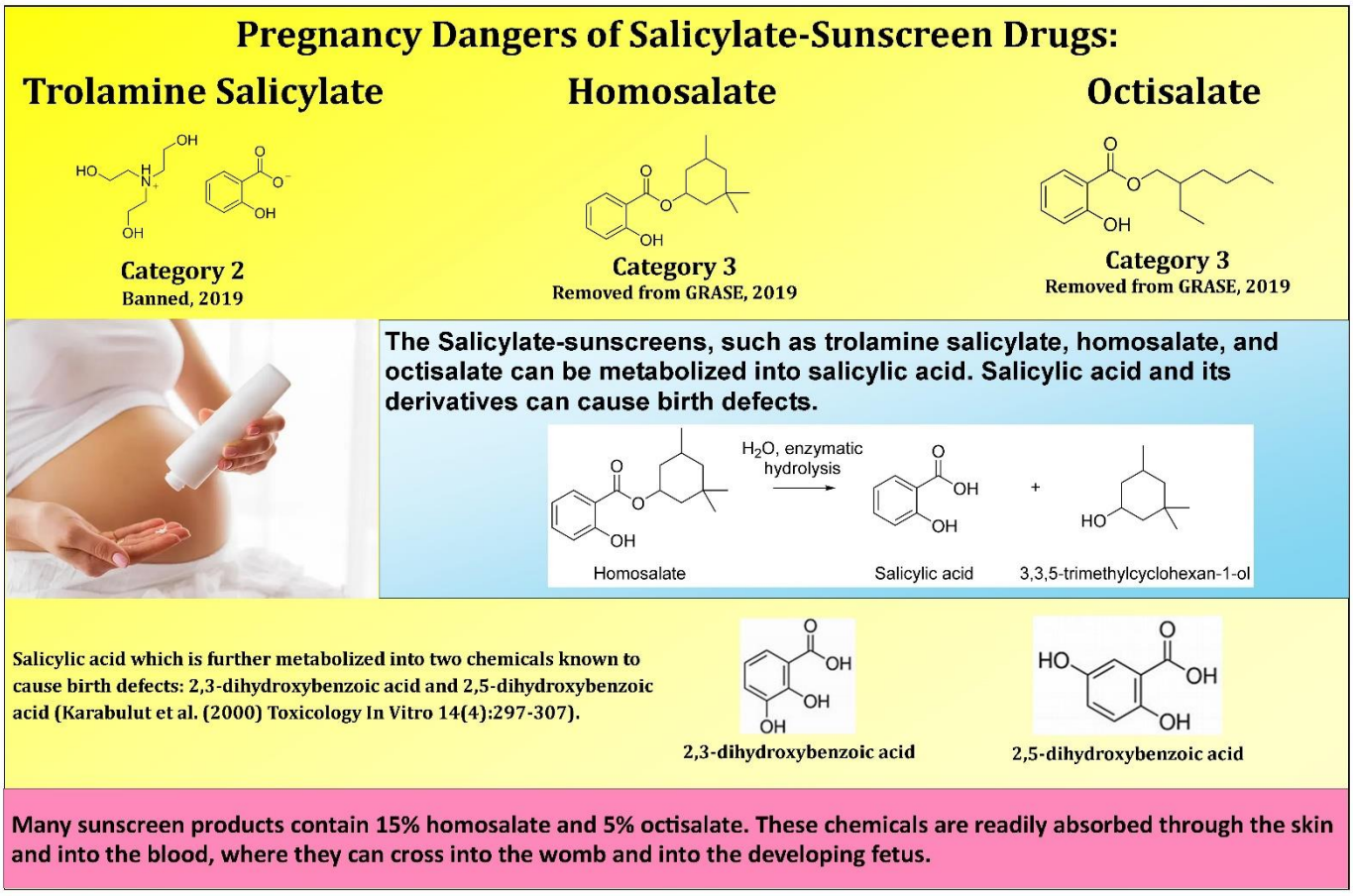
Human Absorption: A maximum octisalate level of 5.8 ng/mL (11.6 times LOC) was observed in the blood; unsafe levels persisted until day 7 (Matta 2020).

Sub-Chronic Toxicity: ECHA (1963b) reports that **"**no clear NOAEL could be determined for systemic effects due to increased incidence in spontaneous nephritis and mild hepatitis". **"**The Lowest Level Adverse Effect Level for systemic

effects was 0.5 ml/kg/day" for methyl salicylate (expressed as octisalate).

Carcinogenicity Concerns: ECHA (1963c) reported oral administered of octisalate produced "gross pituitary gland lesions in 10 rats at 250 mg/kg bw/day compared to 4 rats in the control groups. Incidence in the 500 mg/kg/day group was similar to controls, while all animals of the 1000 mg/kg/day group died before the usual age at which many spontaneous lesions develop".

Reproductive Concerns: Orally, octisalate demonstrated higher post-implantation loss and a reduction in live pups per dam at 250 and 80 mg/kg bw/day. "Reduction in the mean number of pups per dam was statistically significant at the high-dose level whereas reduction in birth index was statistically significant at both dose levels. These effects were considered to be test item related" (ECHA 2012).



Octinoxate (CAS#: 83834-59-7; MW = 290.4 Dalton's):

Human Absorption: A maximum octinoxate level of 7.9 ng/mL (15.8 times LOC) was observed in the blood; unsafe levels persisted until day 7 (Matta 2020).

Pediatric Concerns: Manova (2015) noted that "the predicted aggregate exposure for octinoxate exceeds the Derived No Effect Level for thyroid-disrupting effects such as for children aged ≤4 years, who might be particularly susceptible to endocrine disrupting events". A more complete listing of references relating to octinoxate in vitro and in vivo thyroid toxicity can be found at Regulations.gov, Docket FDA-1978-N-0018 (DiNardo 2019).

Effects on Human Testosterone/Semen/Sperm: octinoxate can negatively impact testosterone levels, as well as mimic the effect of progesterone on Ca^{2+} signaling in human sperm cells, an effect that might impair human fertilization (Janjua 2004, Rehfeld 2016).

Table 1: Comparison of Benzophenone (BP) in samples to FDA Banned Level and EFSA Safe Level in Foods

Product Name/Product Type/Weight Declaration[1]	BP in Product (ppm) unaged/aged	ug/Kg/day[2] unaged/aged	FDA Ban Level ug/Kg/Day	Times Above FDA Ban Level[3]	EFSA Safe Level ug/Kg/Day	Times Above EFSA Safe Level[4]
Coppertone Clear Sunscreen Sport Clear 30 Beach Product - 148 ml (5 fl oz)	185.5/434.9	2164/5074	0.75	**2885/6765**	10	**216/507**
Neutrogena Beach Defense Sunscreen Spray 100 Beach Product - 184 g (6.5 oz)	69.7/101.5	813/1184	0.75	**1084/1579**	10	**81/118**
L'Oreal Age Perfect Soin Rose Re-Fortifiant FPS 20 Anti-Aging Face Product - 50 ml	64.6/193.4	754/2256	0.75	**1005/3008**	10	**75/226**
Coppertone Sunscreen Spray Water Babies 50 Beach Product - 170 g (6 oz)	63.7/101.5	743/1184	0.75	**991/1579**	10	**74/118**
Cosmia Sun BB Creme SPF 50 Haute Protection Anti-Aging Face Product - 50 ml	52.2/72.4	609/845	0.75	**812/1126**	10	**61/84**
Coppertone Kids Sport SPF 50 Spray Beach Product - 208 g (7.3 oz)	36.5/41.8	426/488	0.75	**568/650**	10	**43/49**
Banana Boat Sport Performance Sunscreen Lotion 50+ Beach Product - 236 ml (8 fl oz)	26.6/43.5	310/508	0.75	**414/677**	10	**31/51**
Coppertone Sunscreen Lotion Defend & Care Face Oil Free 50 Beach Product - 88 ml (3 fl oz)	24.8/39.5	289/461	0.75	**386/614**	10	**29/46**
Bioderma Photoderm AR SPF 50+ Teinte Naturelle Anti-Aging Face Product - 30 ml	22.2/32.6	259/380	0.75	**345/507**	10	**26/38**
LaRoche-Posay 50+ SPF Brume Invisible Transparentes Spray Beach Product - 200 ml	15.0/22.9	175/267	0.75	**233/356**	10	**18/27**
Neutrogena Beach Defense Sunscreen Lotion 70 Beach Product - 198 ml (6.7 fl oz)	13.4/20.7	156/242	0.75	**208/322**	10	**16/24**
Cosmia Sun Haute- High Protection SPF 30 Beach Product - 100 ml	11.9/25.7	139/300	0.75	**185/400**	10	**14/30**
Banana Boat Clear UltraMist Sport Performance 30 Beach Product - 269 g (9.5 oz)	11.1/17.7	130/207	0.75	**173/275**	10	**13/21**
LaRoche-Posay Sans Traces Blanches SPF 50+ Anti-Aging Face Product - 50 ml	10.7/15.4	125/180	0.75	**166/240**	10	**12/18**
Garnier Ambre Solaire Resisto Enfant FPS 50+ Beach Product - 200 ml	10.2/22.6	119/264	0.75	**159/352**	10	**12/26**
Uriage Age Protect Fluide Multi-Actions SPF 30 Anti-Aging Face Product - 40 ml	6.3/9.8	74/114	0.75	**98/152**	10	**7/11**
Negative Control - Nivea Sun Protect & Hydrate SPF 50+ Beach Product - 200 ml	0/0 (no octocrylene)	N/A	0.75	**N/A**	10	**N/A**

1) Product Type – Size: is represented as "Beach" if over 50 ml and "Anti-aging" if 50 ml or less. 2) BP in ppm (mg/Kg)/60Kg * 0.7 (70% Absorption) *1000 (mg to ug conversion) = ug/Kg/day 3) ug/Kg/day in product/0.75 FDA ug/Kg/day = Times Above FDA Ban Level 4) ug/Kg/day in product/10 EFSA ug/Kg/day = Times Above EFSA Safe Level

Table 2: Pediatric Considerations Base on the Highest and Lowest Levels of Benzophenone (BP) Determined in Beach Products[1]

Highest BP Level Observed: Coppertone Clear Sunscreen - Sport Clear 30 – 148 ml (Beach Product)

Age	Weight (Kg)	BP in Product (ppm) Baseline/6 Week 40^{0}C	ug/Kg/day[2] Baseline/6 Week 40^{0}C	FDA Ban Level ug/Kg/Day	Times Above FDA Ban Level[3]	EFSA Safe Level ug/Kg/Day	Times Above EFSA Safe Level[4]
2 Yrs	12.5	185.5/434.9	10388/24354	0.75	13851/32473	10	1039/2435
10 Yrs	32.0	185.5/434.9	4058/9513	0.75	5410/12685	10	406/951
Adult	60.0	185.5/434.9	2164/5074	0.75	2885/6765	10	216/507
Adult	75.0	185.5/434.9	1731/4059	0.75	2308/5412	10	173/406

Lowest BP Level Observed: Sample Garnier Ambre Solaire Resisto Enfant FPS 50+ - 200 ml (Child Beach Product)

Age	Weight (Kg)	BP in Product (ppm) Baseline/6 Week 40^{0}C	ug/Kg/day[2] Baseline/6 Week 40^{0}C	FDA Ban Level ug/Kg/Day	Times Above FDA Ban Level[3]	EFSA Safe Level ug/Kg/Day	Times Above EFSA Safe Level[4]
2 Yrs	12.5	10.2/22.6	571/1266	0.75	762/1687	10	57/127
10 Yrs	32.0	10.2/22.6	223/494	0.75	298/659	10	22/49
Adult	60.0	10.2/22.6	119/264	0.75	159/352	10	12/26
Adult	75.0	10.2/22.6	95/211	0.75	127/281	10	10/21

1) Product Type – Size: is represented as “Beach” if over 50 ml.

2) BP in ppm (mg/Kg)/60Kg * 0.7 (70% Absorption) *1000 (mg to ug conversion) = ug/Kg/day

3) ug/Kg/day in product/0.75 FDA ug/Kg/day = Times Above FDA Ban Level

4) ug/Kg/day in product/10 EFSA ug/Kg/day = Times Above EFSA Safe Level

Table 3: Comparative Incidence of Melanoma Australia vs. United States 1982 – 2015

Incidence rates of melanoma of the skin, all ages. Age-standardized rate (world) per 100,000

	Australia			**United States (SEER 9 registries)**		
Year	Males	Females	Both sexes combined	Males	Females	Both sexes combined
1982	20.8	20.7	20.6	9.3	8.0	8.6
1983	21.4	22.3	21.6	9.4	7.8	8.5
1984	23.0	22.3	22.4	9.5	8.1	8.7
1985	24.8	24.5	24.4	11.2	8.8	9.8
1986	26.2	24.2	25.0	11.6	9.2	10.2
1987	30.6	27.3	28.7	11.7	9.6	10.5
1988	33.5	27.9	30.4	11.0	8.9	9.8
1989	31.5	25.4	28.1	12.0	9.3	10.4
1990	31.2	25.2	27.9	12.1	9.3	10.5
1991	30.8	25.7	28.0	12.8	9.7	11.1
1992	34.0	26.9	30.1	13.1	9.5	11.1
1993	34.4	27.1	30.4	13.1	9.4	11.0
1994	35.0	27.2	30.7	14.1	9.8	11.7
1995	37.3	28.5	32.5	14.4	10.7	12.3
1996	37.8	29.4	33.2	15.5	11.0	13.0
1997	39.9	30.9	35.0	15.5	11.4	13.2
1998	36.9	28.2	32.2	15.6	11.5	13.3
1999	38.1	28.6	33.0	16.1	11.8	13.6
2000	38.4	29.0	33.4	16.7	12.0	14.0
2001	38.9	29.2	33.7	17.0	12.7	14.5
2002	42.0	31.0	36.1	16.6	12.5	14.2
2003	40.1	28.8	34.1	16.8	12.6	14.4
2004	39.6	30.0	34.4	17.5	13.3	15.1
2005	42.2	32.1	36.8	19.3	14.1	16.3
2006	41.0	28.4	34.3	19.1	14.0	16.2
2007	39.1	28.5	33.4	18.4	13.7	15.7
2008	40.9	29.2	34.7	19.5	14.4	16.6
2009	40.5	28.8	34.3	19.6	14.1	16.5
2010	40.2	28.1	33.8	19.8	14.8	16.9
2011	39.7	28.2	33.6	18.9	14.0	16.1
2012	40.5	28.8	34.3	19.4	13.7	16.2
2013	41.1	29.4	34.9	20.1	14.4	16.9
2014	40.7	29.7	34.8	20.9	15.1	17.6
2015	41.7	30.1	35.6	20.9	15.8	18.0
Delta %	**100%**	**45%**	**73%**	**220%**	**161%**	**192%**

SOURCES: Data provided by the American Cancer Society

Australia: Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: melanoma of the skin Canberra: AIHW. <https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/>.

United States: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Research Data, Nov 2018 Sub (1975-2016) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969-2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2019, based on the November 2018 submission.

Delta % (Percent Change from Baseline) **=** data for 2015 – data for 1982/data for 1982 * 100

Cancer Proliferation Concerns: Several studies report on the cellular proliferation of human MCF-7 and MDA-MB-231 cells demonstrating an increase in the migratory and invasive properties of octinoxate using several different in vitro assays at a variety of concentrations. (Alamer 2018, Duale 2010, Schlumpf 2001, Schlumpf 2004).

Note: Oxybenzone has been reported in some of the references above to also proliferate human breast cancer cells in vitro.

Avobenzone (CAS# 70356-09-1; MW 310.4 Dalton's):

Human Absorption: A maximum octisalate level of 7.1 ng/mL (14.2 times LOC) was observed in the blood; unsafe levels persisted until day 7 (Matta 2020).

Endocrine Disrupting Chemical (EDC) Synergy: Avobenzone can produce an endocrine disrupting effect when combined with other endocrine disrupting sunscreen actives and personal care product ingredients below the NOAEL for each chemical individually. The same holds true for the sunscreen actives meradimate, octisalate, homosalate, octyl dimethyl PABA, oxybenzone, octocrylene, and octinoxate (Rehfeld 2016).

Carcinogenicity Concerns: A clinical sunscreen use trial was conducted in Nambour Australia (Green 2011) with findings of a 50% reduction in melanoma and a 40% reduction in squamous cell carcinoma (SCC). One group (812 participants) received an unlimited supply of a SPF 16 broad-spectrum sunscreen (for the first 4.5 years) containing 8% octinoxate and 2% avobenzone. A second group (809 participants) were not given a product to use, but were allowed to continued using sunscreen if desired.

First, the group showing a reduction in skin cancers were given a sunscreen with a combination that is known to be photo-unstable (FutureDerm 2012). Second, at the time of the study (1992 to 2006) the incidence of melanoma in Nambour was 71/100,000 people and according to an Australia Institute report (2019) the current rate of melanoma is now 72/100,000 people. Third, the group not receiving sunscreen had twice as many people enrolled in it that had a history of skin cancer, contained people that burned more readily and had lighter skin color, work outdoors more, had more outside leisure activities, a greater history of burns and more naevi on their backs - all known predispositions for skin cancer. Forth, 87 unexplained deaths occurred in the group given a sunscreen vs. 86 unexplained deaths in the discretionary use group.

It is unclear what the value of a 50% reduction in melanoma is, in a location that demonstrates no change in the incidence of melanoma over time, using a photo-unstable sunscreen for 4.5 years, in a study that had a total of 173 unexplained deaths out 1,621 participants and matched to a control group with a greater predispositions for skin cancer? SCCs are not tracked in a similar manner as melanoma, but these findings should cause one to question the 40% reduction in SCCs observed as well.

On a similar note, Table 3 compares the incidence of melanoma (1982 – 2015) for all of Australia and the United States. A consistent increase is clearly evident demonstrating the complexity of the problem while asking the question do sunscreens meet the requirements for safety and effectiveness?

Putting Numbers Into Perspective:

This communication discusses most, but not all, of the organic sunscreens that have been removed by the FDA from Category I; all of which have a MW below 500 Dalton's allowing them to easily pass through the skin into the blood and the placenta barrier (Bos 2000, Wilson 2007). The six most common actives discussed can be used in combination at maximum levels yielding a potential product with a total of 46.5% actives. To date no systemic toxicity studies have been conducted on a product that contains these levels. Extrapolating the FDA absorption data (Matta 2020) for these six actives would produce a total maximum absorption potential of 309.8 ng/ml, which is 619.6 times above the LOC for systemic toxicity.

Additionally, this review does not cover the environmental impact of sunscreens, which is extensive to say the least. Carve et al (2020) conducted a review of 89 such studies and concluded that moderate to high-risk hazard quotients exists for several of these actives.

Lastly, it is important to point out that this commentary only discusses a small portion of toxicological studies published. Regardless, it is the hope of the authors that there is enough data presented that makes it clear why FDA considers the organic sunscreens either not safe for human use (Category II) or more data is needed (Category III) to determine human safety/efficacy and why a definitive guideline like the Sunscreen Innovation Act is needed for industry guidance and for the protection of all sunscreen users.

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