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# Sunscreen Chemicals Found in the Bloodstream: Expert Reaction

>> Chemicals found in different sunscreens enter the bloodstream at levels that far exceed the FDA's recommended threshold for requiring toxicology studies, according to a new study in *Journal of the American Medical Association*.

Leading dermatologists reviewed the new findings for *Practical Dermatology*® magazine and are quick to caution that the benefits of using sunscreen far exceed any documented downsides. (See what a study author has to say about the findings on page 12.)

"The last thing we need is for patients to panic and stop using sunscreen, says San Diego-based dermatologist Neal Bhatia, MD, Chief Medical Editor of *Practical Dermatology*® and Vice President-Elect of the AAD. "This is a small lab-based maximum use study of 24 subjects who used sunscreen four times a day for four days. These lab results do not translate to the real world and should not change our practice in any way. 'Plasma detected' also does not directly translate to 'toxic,' so nobody should overreact, and the investigators also said that sunscreen use should not be stopped. We have been using and recommending sunscreens with these chemicals for decades without any safety signals.

"By the way, skin cancer is not a great alternative," he adds.

In the study, 24 participants applied one of four different kinds of sunscreen spray, lotion, or cream four times per day for four days on about 75 percent of their body surface area. Researchers then measured the concentration of avobenzone, oxybenzone, octocrylene, and ecamsule in the blood. If the blood absorption of any of these ingredients exceeds 0.5 nanograms per milliliter (ng/mL), the FDA recommends that they undergo nonclinical toxicology assessment, including systemic carcinogenicity and additional developmental and reproductive studies.

The levels of all four chemicals in the participants' bloodstreams far exceeded that within one day—and three remained there for seven days. For oxybenzone, in particular, plasma concentrations reached the threshold within two hours after a single application and exceeded 20ng/mL on day 7 of the study. The FDA has previously included these four chemicals on a list of ingredients that need to be researched further before they can be considered "generally safe and effective."

Hawaii, the Pacific nation of Palau, and Florida's Key West recently banned sunscreens containing oxybenzone and octinoxate on the controversial grounds that they may cause coral bleaching and are dangerous to marine life.

"Ultraviolet radiation causes skin cancer. Therefore a comprehensive sun protective regimen which includes sunscreen, sun avoidance, and protective clothing is central to prevention," says Adam Friedman, MD, FAAD, Professor and Interim Chair of Dermatology at George Washington School of Medicine and Health Sciences in Washington, DC, where he also serves as Residency Program Director, Director of Translational Research and Director of Supportive Oncodermatology.

"These data do not suggest that individuals should refrain from using sunscreen," stresses Dr. Friedman. "While these data certainly suggest that the systemic absorption of sunscreens should be evaluated, these findings cannot be correlated to toxicity or pathology." Furthermore, he says, the experimental protocol was for optimal use which is not the same as real-world use.

"The number of those evaluated was low (six per group) and did not account for all skin types and external environments, which do play a role in barrier integrity," Dr. Friedman says.

## CONSIDER MINERAL-BASED SUNSCREENS

Joshua Zeichner, MD, Director of Cosmetic and Clinical Research in the Department of Dermatology at The Mount Sinai Hospital in New York City, agrees. "In the real world, consumers do not apply as much sunscreen as they should or reapply every two hours, so it is unclear whether there is absorption with every day, real-world use."

More data is clearly needed, he says. "Based on what we know today, the benefit of wearing sunscreen in protecting the skin against skin cancer and premature aging outweighs the potential risks."

Alternatives to these chemical blockers do exist. "If anyone is concerned with the use of chemical blocker sunscreens, mineral options that contain zinc oxide alone or in combination with titanium dioxide are a great option," Dr. Zeichner adds.

"These sunscreen ingredients have been used for several decades without any reported internal side effects in humans," echoes AAD President George J. Hruza, MD, in a statement. "Skin cancer is the most common cancer in the United States, and dermatologists see the impact it has on patients' lives every day. Unprotected exposure to the sun's ultraviolet rays is a major risk factor for skin cancer."

## DON'T DISMISS THESE FINDINGS

Joel Schlessinger, MD, FAAD, a dermatologist and general cosmetic surgeon in Omaha, Nebraska and Chief Cosmetic Surgery Editor of *Practical Dermatology®* magazine, is concerned that merely dismissing these study findings will backfire. "We as dermatologists will always live, eat, and breathe the concept of sunscreen. It is safe and certainly safer than sun exposure, but we have to be cognizant of what is in the media," he stresses. "These concepts are being espoused by extremist environmental groups and now the FDA," he says. "We have to recognize that reef-safe sunscreens and consideration of whether these chemicals do get absorbed in the bloodstream matters to our patients."

Instead of deconstructing the research, dermatologists should educate interested patients about available chemical-free, mineral-based sunscreens, he suggests.

"This also may be an opportunity to exert more pressure on the FDA to revisit the addition of new sunscreen ingredients to the space," he notes.


## FDA APPROVES SORILUX FOR ADOLESCENT PLAQUE PSORIASIS

The FDA has approved Mayne Pharma Group Limited's Sorilux (calcipotriene) Foam, 0.005% in adolescents 12 years and older. The FDA approved Sorilux in 2010 based on evidence from two eight-week placebo controlled clinical trials in patients with mild to moderate plaque psoriasis of the body and one eight-week placebo controlled clinical trial in patients with moderate plaque psoriasis of the scalp. Further data was obtained in a follow-on open label study in patients aged 12 to 17 years of age with psoriasis.

## OBAGI LAUNCHES SKINCLUSION INITIATIVE

Obagi kicked off its SKINCLUSION initiative, designed to elevate the global dialogue about diversity and how we can all make conscious choices to see the beauty in all of our differences, with an event in New York City introducing Priyanka Chopra Jonas as its SKINCLUSION ambassador.

Obagi President Jaime Castle says the company developed this initiative to focus on the need for people to be fully inclusive and to help people recognize their own unconscious biases, especially surrounding skin tone. At the launch event, she introduced a panel of female leaders who have pledged their careers to diversity inclusion, including Ms. Chopra Jonas; Josipa Palac, International Cultural Diversity Organization's (ICDO) President and CEO; Elizabeth L. Haines, PhD, a research scientist for Project Implicit and a professor and director of the Social Cognition Lab at William Paterson University; and Jeanine Downie, MD, director of Image Dermatology P.C. in Montclair, NJ.

"Obagi's SKINCLUSION initiative represents our commitment as leaders in the skincare space to elevate the global dialogue about diversity and inclusion, and spark actions that are more inclusive and reflective of all of our beautiful differences," says Ms. Castle.

ICDO is a Vienna-based global nonprofit dedicated to promoting peace, humanity, diversity and interculturality. ICDO challenges cultural misperceptions to ensure equal participation of every individual or group within society. By bringing attention to different cultural expressions and values, ICDO encourages cultural interaction and connects people by closing cultural gaps.

"Through everyone's participation in the initiative and Obagi's generous support, ICDO will continue to host new and innovative programs around the world that celebrate our multicultural differences and promote a true understanding of humanity," says Ms. Palac.

Project Implicit is a virtual laboratory and research organization developed by behavioral scientists to provide education about implicit bias through Implicit Association Tests (IATs), which is designed to reveal our biases toward various social groups. Individual results are private and become part of ongoing collective research results.

Obagi was the first medical skincare brand to design its clinical research protocols to cover all six skin types across the Fitzpatrick skin spectrum. Obagi believes that protecting and n

"I am delighted to see that Obagi is putting its commitment to diversity and inclusion front and center," says Dr. Downie. "The reality is that not all skin tones are the same when it comes to determining what kinds of products and treatments are effective. The fact that the team at Obagi has ensured their clinical trials are designed to include skin types across the entire Fitzpatrick skin spectrum is significant and should be the way forward for the entire skincare industry." She encourages all skincare companies to do research on skin types I-VI, to have an ethnically diverse staff, and to include all ethnicities in their marketing campaigns.

At SKINCLUSION.com individuals can view resources from the ICDO and Project Implicit, and take the Skin Tone Implicit Association Test. Dermatologists can join the global dialogue celebrating diversity and inclusion by using #SKINCLUSION on social channels and share why diver-

sity and inclusion are important to them; watch, like, and share Priyanka's SKINCLUSION video to keep spreading the word. For every social action taken using #SKINCLUSION, Obagi will donate $1 to support the ICDO and Project Implicit, with a total donation up to $150,000.

## NESTLÉ ENTERS INTO NEGOTIATIONS TO SELL NESTLÉ SKIN HEALTH

Nestlé has entered into exclusive negotiations with a consortium led by EQT and a wholly owned subsidiary of the Abu Dhabi Investment Authority (ADIA) for the sale of Nestlé Skin Health for a value of CHF 10.2 billion. Nestlé Skin Health had net sales of CHF 2.8 billion in 2018. The proposed transaction will be subject to employee consultations and approval of regulatory authorities and is expected to close in the second half of 2019. The company will provide an update on the use of proceeds and its future capital structure at that time.

## NEW NRS STUDY: TREATMENT IMPROVES LIVES

Treating rosacea can have a major positive impact on patients' lives, according to a new survey by the National Rosacea Society. In the survey of 1,044 rosacea patients, around 76 percent of all respondents saw at least some improvement in their skin after receiving treatment. Among those patients, 40 percent said that treatment had improved their psychological well-being, 35 percent said their social well-being had improved, and 31 percent saw improvement in their occupational well-being.

When the signs and symptoms of rosacea are virtually eliminated, however, the improvement in patients' lives was often dramatic, the survey found. Eighty-one percent of those

# close up

**With David Strauss, MD, PhD**

Media coverage of the *JAMA* study suggesting that sunscreen chemicals can travel to the bloodstream combined with a growing movement to protect the coral reef by banning certain sunscreen chemicals left many patients wondering about the safety of these products and many dermatologists worried that patients would simply stop using sunscreen as a result. The man behind the FDA study, Dr. David Strauss, director of the division of applied regulatory science at the Center for Drug Evaluation Research at the FDA, spoke to *Practical Dermatology®* about the implications of the study.

### Why is this topic important to study?

**David Strauss MD, PhD:** Sunscreens prevent skin damage by reflecting, absorbing, and/or scattering UV radiation and are regulated as over-the-counter (OTC) drug products in the US. For some individuals, sunscreen products may be applied in substantial amounts multiple times every day over the course of a lifetime as both primary sunscreen products, starting from an age of six months, and as ingredients in cosmetic products. It was previously not known whether many sunscreen active ingredients are absorbed systemically.

### Describe the research and your findings.

**Dr. Strauss:** This randomized clinical trial demonstrated systemic exposure of four commonly used sunscreen active ingredients on application of sunscreen products under maximal use conditions consistent with current sunscreen labeling. All four sunscreen active ingredients tested resulted in systemic exposure. The clinical effect of systemic exposure is unknown, necessitating further research. These results do not indicate that individuals should refrain from the use of sunscreen.

### What is the next step?

**Dr. Strauss:** FDA has recently issued a proposed rule to update regulatory requirements for most sunscreen products available in the US. As part of this rule, we are asking industry and other interested parties for additional safety data regarding the absorption of 12 of the 16 active sunscreen ingredients currently available.

A second phase of the study just released in *JAMA* will use a different design to investigate additional questions raised by this study, including the maximum plasma concentration after a single application, the skin concentration during the washout phase, the plasma concentration up to 17 days after the last dose, and the systemic exposure to additional commonly used sunscreen ingredients. In addition, larger "maximal usage trials" are needed to better delineate the absorption of sunscreen active ingredients over the larger population that uses sunscreens. Finally, nonclinical toxicology studies are warranted that include systemic carcinogenicity and additional developmental and reproductive studies. ■

who had achieved clear or almost clear skin said their psychological well-being had improved. Seventy-one percent said successful treatment had also improved their social lives, and 62 percent reported improvement in their occupational well-being.

In contrast, among patients whose rosacea was only slightly or moderately improved, only 24 percent of respondents reported improved psychological well-being, only 21 percent felt their social lives had improved, and just 19 percent said they were better off at work. ■

## Take 5 with Almirall President and GM Ron Menezes

**Exhibiting at the AAD Annual Meeting was far different for Almirall this year than in 2018.**

**In 2018, when Almirall was a new name in the US market and the company's drug portfolio was slim, "Nobody came around our booth," says Ron Menezes, President and General Manager. A year later, the company had name recognition, a novel drug approval, and a recently acquired stable of medical dermatology drugs from Allergan, resulting in, "an incredible amount of traffic," Mr. Menezes says.**

**Founded in 1943, Almirall is the largest pharmaceutical company in Spain and an industry leader in Europe. It entered the US market with the acquisition of Aqua Pharmaceuticals in 2013. The company rebranded as Almirall in the US in October 2018. Almirall US is headquartered in Exton, PA. Mr. Menezes sees Almirall as the leading dermatology pharmaceutical company in the US within 10 years. He spoke to *Practical Dermatology*® about the company.**

### 1. The Focus is Medical Dermatology

**Ron Menezes:** We have close to 300 scientists at the global headquarters in Barcelona, focused on medical dermatology. In addition, we've done multiple agreements with different companies, for assets in early development.

Aesthetics is a very tough environment. Very competitive. Very high cost to get in. High cost to stay in. We made a decision in mid-to-late 2018 to divest the aesthetics business and, as I like to say, "double down," in medical dermatology.

We are redirecting all resources right to medical dermatology. We are now focusing in disease states like atopic dermatitis, psoriasis, and alopecia. A disease state I'm passionate about is acne. And a lot of companies are walking away from acne. But I think if you come out with something innovative, there's opportunities out there. And if you are conservative in the pricing, there are opportunities from that perspective.

### 2. Innovation is Key

**Mr. Menezes:** The key to the future is not another product that has a different way of delivering the same product or active ingredient as somebody else. It is really innovation.

We're here because I think there's a vacuum in leadership right now in medical dermatology driving innovation.

What you just saw with the launch of sarecycline is innovation. That is the first unique oral novel antibiotic in the market in 40 years. It's the first new chemical entity for acne in 10 years. The last one was topical dapsone, which we also have.

### 3. The Dermatology Community is Excited

**Mr. Menezes:** In October 2018 we launched the Almirall sales force, knocking on doors with samples, with things that can help lower the cost for patients. We did a lot of things quickly to get our acquired drugs in front of physicians. And there was a lot of excitement.

We had to remind dermatologists that we also have other products—legacy Aqua Pharmaceuticals products—that still are out there. They're great products.

It really has been a nice way to bridge the future from legacy Aqua Pharmaceuticals, all the way to the future of innovation that will be coming in early 2021.

### 4. Almirall's Investigational AK Agent is Promising

**Mr. Menezes:** At the annual meeting of the AAD we presented 57-day data for KX2-391 [also known as KX-01, developed in collaboration with Athenex], a first-in-class dual Src kinase and tubulin polymerization inhibitor.

That's the kind of innovation we're looking for. In the future, we will look to present data to ensure that these products are covered by third-party payers. We anticipate a possible submission to the FDA in the next year.

### 5. AlmirallShare is Creating Opportunities

**Mr. Menezes:** AlmirallShare is truly an I&D platform. Right now, we have over 450 scientists registered and over 170 proposals. This was set up in late 2017. This is 100 percent done through the R&D team back in Barcelona, that reviews the proposals.

This is an opportunity—from scientists, from students in medical school—anybody who comes up with an idea. If you're approved, you get funding, with different ranges available. I'm excited, because there have been a couple of ideas that came out. They're already moving forward. But they give an opportunity for someone to get access to funding, short of the normal routes. It may help us find the new molecule that will help a patient with atopic dermatitis, a patient with acne, or another skin condition that's not been treated before.

## CROWN LABORATORIES ADDS TO PORTFOLIO; UPDATES BRANDING

On the heels of a brand relaunch, Crown Laboratories' Aesthetics division, Bellus Medical, has acquired the HD PRP system for the aesthetic marketplace from Healeon Medical, Inc. The system is designed to meet the demands of busy practices seeking higher volume and higher yield Platelet Rich Plasma procedures. As part of their expanding Platelet Rich Plasma portfolio, Bellus Medical says it will re-brand its suite of offerings as the ProGen PRP Advantage and ProGen PRP Versa lines; both high-yield systems for use in Platelet Rich Plasma procedures.

CROWN
SKIN SCIENCE FOR LIFE

Crown also has acquired Xycrobe Therapeutics, Inc. Xycrobe's technology focuses on utilizing the ubiquitous nature of skin microbes by turning them into vehicles for the delivery of biotherapeutics.

Crown intends to explore use of the Xycrobe technology across its brand portfolio, including its Bellus Medical, Vita Liberata, and Consumer divisions.

Crown's new tagline 'Skin Science for Life' highlights the company's focus on aesthetic medicine, generic and branded dermatological prescription drugs, OTC and prestige beauty.

Along with the tagline, the company's new logo incorporates a multicolor palette which symbolizes Crown's revitalized spirit, energy and excitement in its pursuit of scientific excellence in the skin care arena.

## DERMAVANT FILES FOR $100M IPO

Dermavant Sciences recently filed with the SEC to raise up to $100 million in an initial public offering, Renaissance Capital reports.

The company, a dermatology-focused subsidiary of Roivant Sciences, has made several key appointments lately, including naming Todd Zavodnick Chief Executive Officer.

In a recent interview, Mr. Zavodnick said Dermavant as a company, "genuinely excites me." The lead asset, tapinarof, is an investigational non-steroidal preparation being developed for atopic dermatitis. Other product candidates in the pipeline may address atopic dermatitis, hyperhidrosis, vitiligo, and acne.

"Dermavant is a biotech company that we aim to operate within medical dermatology and deliver innovation," Mr. Zavodnick said. "We understand what patients and healthcare providers need in today's market. We also understand access and what managed care is going to mean to the United States in the years coming, and the novel approaches it will require to ensure new medicines reach patients easily."

## POSITIVE 90-DAY RESULTS FROM CONFORM STUDY: RECROS

Ninety-day results from the CONFORM study assessing the efficacy, safety, and patient satisfaction of the Rotational Fractional Resection (RFR) procedure for submental contouring are promising. RFR is a novel, proprietary alternative to traditional approaches to treat skin laxity developed by Recros Medica, Inc. Hema Sundaram, MD, FAAD presented the study results at the 2019 American Society for Aesthetic Plastic Surgery (ASAPS) meeting.

In the CONFORM study, adults with mild to moderate skin laxity and excess fat were treated to improve submental contouring. At baseline, 99% of subjects were dissatisfied with their neck and jawline appearance, while at 7-days after a single RFR procedure, 84% were now satisfied. Satisfaction with the appearance of the neck and jawline persisted and at the 90-day timepoint was 82% which represented a statistically significant change from baseline. In addition, 94% of patients at Day 90, indicated they were likely to recommend this procedure to friends and family.

## CONSTELLATION ALPHA CAPITAL TO MERGE WITH DERMTECH

Constellation Alpha Capital Corp. is merging with DermTech, Inc., a molecular genomics company with an initial focus on skin cancer.

"DermTech has developed a deep pipeline of dermatology-focused

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diagnostic tests with superior clinical sensitivity, improved patient comfort due to non-invasive sample collection and meaningful cost savings for payors. We are excited to bring this potential opportunity to our shareholders," says Mr. Rajiv Sarman Shukla, Chairman and Chief Executive Officer of Constellation, in a news release. "DermTech has developed a deep pipeline of dermatology-focused diagnostic tests with superior clinical sensitivity, improved patient comfort due to non-invasive sample collection and meaningful cost savings for payors. We are excited to bring this potential opportunity to our shareholders." ■