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US FDA's Proposed Sunscreen Order Due With Inquiry Ongoing Re Environmental Impacts

by Ryan Nelson

Industry anticipates a proposed administrative order from the US FDA by 27 September on OTC sunscreen drug products, including GRASE status of active ingredients. Meanwhile, the agency's probe continues into UV filter environmental impacts, and the National Academy of Sciences is gathering information to weigh those possible ills against human health consequences of reduced sunscreen use.

UV filters are under intense scrutiny the world over, not only with respect to their human health effects but also their environmental impacts, creating a haze of uncertainty over the sunscreen products category.

In the US, the Food and Drug Administration is expected to issue a proposed order on sunscreens by 27 September, as required by the Coronavirus Aid, Relief and Economic Security (CARES) Act, which President Donald Trump signed into law in March 2020.

The CARES Act included a rider for long-sought reforms to the FDA's OTC drug review program, shifting the monograph development process from cumbersome notice-and-comment rulemaking to a nimbler administrative process with timelines for FDA decisions.

It also wiped the slate clean for sunscreen ingredients designated Category III in a tentative final monograph for sunscreen drug products issued by the FDA in February 2019. Category III comprises ingredients in need of additional data to support decision making as to their generally recognized as safe and effective (GRASE) status, which dictates OTC monograph inclusion. (Also see "*CARES Act Makes Threatened Sunscreen Ingredients GRASE Again, But Next Steps Uncertain*" - HBW Insight, 15 Apr, 2020.)

According to the FDA's 2019 TFM, a dozen UV filters, including the most commonly used chemical filters for OTC sun protection, were in need of data to continue to be recognized as GRASE. Only zinc oxide and titanium dioxide, both physical UV blockers, were deemed outright GRASE.

The agency cited findings that oxybenzone and other sunscreen ingredients are absorbed through skin to a greater extent than previously understood, as well as consumers' increased exposure through daily use of sunscreen products, among reasons for requesting updated data. (Also see "*'Data Gaps' Keep 12 Ingredients Off FDA's Proposed OTC Sunscreen Monograph*" - HBW Insight, 21 Feb, 2019.)

While the CARES Act provided a reset, classifying Category III sunscreen ingredients again as GRASE, industry believes the FDA's imminent proposed order could reprise the position it set forth in the 2019 TFM.

> ***How and by what statutory mechanism could the FDA's environmental assessment factor in OTC sunscreen decision making? "That question is really the crux of this whole issue," PCPC's Davies said.***

Tom Myers, executive vice president, legal, and general counsel at the Personal Care Products Council, told HBW Insight on 17 September that "every indication we have so far is that the order is going to issue on September 27."

And it's a good bet that the proposal will strongly resemble the TFM from 2.5 years ago, he said.

"Prior to the enactment of the CARES Act and OTC reform, FDA put a tremendous amount of time, energy and resources into developing the 2019 TFM, so it's reasonable to expect that that particular pathway or recourse is open to them, and we could see a proposed administrative order that looks very similar to the TFM," Myers said.

He noted that 18 months have passed since the CARES Act's enactment, theoretically giving the FDA time to craft a substantially revised proposal for governing OTC sunscreen drug products.

However, the agency has had its hands full with the COVID crisis and resource and process development for the new OTC drug program in general. (Also see "*At US FDA, Adding 'Effective'*

Staff For Overhauled OTC Monograph Program 'Really Takes Time'" - HBW Insight, 2 Sep, 2020.)

"So I think they've had other things occupying their time," Myers said. At any rate, "the fact that they had a TFM back in 2019 that already was a very complex, very comprehensive overhaul of the sunscreen monograph, which has already been through internal review and legal review and approval before being issued – given the vast amount of work they put into that – it seems reasonable to think that they would issue an administrative order that looks like that."

He added, "I think the real question is whether or not the FDA will modify the order to reflect comments they received from stakeholders on the TFM."

While the pandemic has inhibited industry's progress somewhat, Myers and PCPC senior colleagues said industry has remained hard at work to produce data previously requested by the FDA to support GRASE decision-making for sunscreen ingredients.

"There's been a great deal of clinical and non-clinical work going on over the past two years. We have not been idle," Myers said.

Alex Kowcz, the trade association's chief scientist, said an industry consortium already has delivered a substantial amount of preclinical data to the FDA, as well as human dermal safety studies, as it progresses toward the maximal usage trials (MUSTs) that the FDA maintains are necessary to assess sunscreen ingredient absorption through skin and bioavailability. (Also see "*FDA's Follow-Up Sunscreen Trial Shows More Of The Same: Absorption Of All Tested UV Filters*" - HBW Insight, 21 Jan, 2020.)

MUST results, in turn, could signal need for additional systemic toxicity testing.

"We are definitely working very hard, and we have many activities ongoing right now across a number of technical workstreams," Kowcz said.

Coral Or Humans?

Meanwhile, the FDA continues to weigh whether an environmental impact statement (EIS) is needed before it issues a final sunscreen order addressing OTC use of sunscreen ingredients.

The National Environmental Policy Act (NEPA) requires agencies to consider the potential environmental consequences, and any reasonable alternatives, prior to implementing any major federal action.

The FDA in May issued a notice of intent to prepare the EIS, citing reports in recent years linking oxybenzone and octinoxate to potential harmful effects on coral reefs. (Also see "*Including Oxybenzone, Octinoxate On US Sunscreen Monograph Could Swing On Environmental Impact*" -

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HBW Insight, 12 May, 2021.)

In 2017, seminal research led by Craig Downs, executive director of the Haereticus Environmental Laboratory in Clifford, VA, started Hawaii on its way to banning the sale of sunscreen products containing oxybenzone and/or octinoxate, legislation that went into effect in January. (Also see "*Hawaii Bills Seek Ban On Oxybenzone-Containing Sunscreens*" - HBW Insight, 14 Feb, 2017.)

In *comments* to the FDA, the Personal Care Products Council and Consumer Healthcare Products Association questioned the need for a sunscreen EIS under NEPA and related FDA regulations. They point to exclusions under federal regs for actions determined by an agency – "on the basis of a shorter 'environmental assessment'" – not to have a significant effect on the environment.

OTC monograph actions are excluded, the trade groups say, "if the action increases the use of the active moiety but the estimated concentration of the substance at the point of entry into the aquatic environment will be below 1 part per billion."

Recent *studies* undertaken by PCPC and University of Maryland environmental scientists showed that neither oxybenzone nor octinoxate are likely to reach or exceed the 1 ppb concentration threshold.

The same team was behind a *paper* published earlier this year in Environmental Toxicology and Chemistry, "A Critical Review of Organic Ultraviolet Filter Exposure, Hazard, and Risk to Corals," in which PCPC and partner scientists conclude "there is limited evidence to suggest that [UV filters'] presence is causing significant harm to coral reefs."

However, the researchers say, "based on the current data set, it would be premature to conclude that environmental concentrations of UV filters do not adversely impact coral reefs."

They identify environmental exposure and fate, toxicity testing, and risk assessment as three areas where additional investigation is needed.

Iain Davies, senior environmental scientist at PCPC, who lists as an author on both papers, summarized the situation. "There's a lot that we don't know, and we do have research ongoing to answer those questions. But there are issues with some of the coral toxicity data that have been used to basically push forward state legislation and have been mentioned in the EIS process. They're just not reliable."

Asked how and by what statutory mechanism an FDA environmental assessment could factor in sunscreen ingredient GRASE decisions, Davies replied, "That question is really the crux of this whole issue."

Myers agreed. Put another way, he said, “how do we evaluate the correlation between coral reef [impacts] and the potential public health impact of limiting access to sunscreen?”

That quandary is being tackled by the National Academy of Sciences, which *has formed an ad hoc committee* to review the state of science on use of sunscreen ingredients currently marketed in the US, their fates and effects in aquatic environments, and the potential public health implications of reduced sunscreen use.

For the time being, it’s unclear how UV filter environmental considerations could feed into the FDA’s OTC sunscreen regulatory work, which – like all FDA activity – is focused fairly strictly, in accordance with the agency's mission, on protecting human health.

Davies said he suspects that the NAS project will have a big influence.

Exactly how is unknown. Myers hypothesized that “the only way it will have an impact, from a regulatory perspective, would be if the environmental impacts were such that they presented some type of human health risk as well through the exposure pathway.”

Benzene, Now Benzophenone?

Putting aside questions about the human health and environmental effects of ingredients intentionally used in OTC sunscreen products, the category also is under attack for toxic contaminants allegedly detected in popular sunscreen offerings.

In May, Valisure LLC, "the pharmacy that checks," announced findings of carcinogenic benzene in leading sunscreen spray products. The report triggered a rush on testing labs, product recalls, class action litigation against named brands, even legislation in Congress to improve supply chain transparency. (Also see "*US Rep. Schakowsky Wants Cosmetic Supply Chain Transparency; Benzene In Sunscreen Cited*" - HBW Insight, 30 Jul, 2021.)

Myers observed, “FDA is aware it [benzene] may be found in food and drugs at certain levels. That’s why they have guidance on levels of residual solvents.” (Also see "*Two ‘Hot Buttons’ Right Now In Product Testing: Benzene In Sunscreens, PFAS In Cosmetics*" - HBW Insight, 23 Jun, 2021.)

He continued, “Certainly we support that guidance and activities to monitor and ensure that companies are conforming with those recommendations at those levels. Having said that, no member company has involved us in their internal discussions or investigations into the root cause, so I couldn’t even opine on where they might stand.”

Another potential contaminant in sunscreen products has received media attention in recent weeks – benzophenone – a mutagen, carcinogen and endocrine disruptor, unrelated to benzene, which Downs of Haereticus says can accumulate in commercial sunscreen products over time as

octocrylene content degrades.

“The safety of octocrylene as a benzophenone generator in SPF or any consumer products should be expeditiously reviewed by regulatory agencies,” say Downs, et al., in the *study* published in August in Chemical Research in Toxicology.

Kowcz noted, “We know at the moment that the study does say that. But we stand behind the safety of octocrylene. All of the regulatory agencies we know about conclude that octocrylene is safe. And the levels they found [in the benzophenone study] have not been confirmed.”

Without additional scientific context, Kowcz said, “it perpetuates misinformation and really misleads consumers about the safety of sunscreen products. And the most important thing here to remember is that sunscreens have a very important [public health] benefit.”

Myers was of a similar mind. “Yes, there’s a lot of attention being paid to sunscreens currently, both in the media and other places. But let’s not forget that these ingredients are all GRAS/GRASE, FDA has approved them all for use, and they [FDA] are being thoughtful in their approach.”

He concluded, “At the end of the day, I think the evidence is going to be very clear that these are safe, and these products have always been safe. Further, they’re needed to prevent another public health crisis, the incidence of skin cancer all around the world.”