November 26, 2007

Comments from Environmental Working Group
on the U.S. Food and Drug Administration's
Proposed Amendment of Final Monograph for Sunscreens

Docket: Sunscreen Drug Products for Over-the-Counter Human Use; Proposed Amendment of Final Monograph
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The Environmental Working Group (EWG) is a non-profit public health and environmental research and advocacy organization based in Washington, DC. We have conducted research on the safety of ingredients in personal care products for the past six years. Among our projects in this area is an investigation of the safety and efficacy of more than 800 name-brand sunscreens (EWG 2007a), published at http://www.cosmeticsdatabase.com/sunscreens.

Background and overview of EWG comments

On August 27, 2007 the U.S. Food and Drug Administration (FDA) published proposed amendments to the final monograph for sunscreen drug products for over-the-counter human use. FDA has published this document in various versions beginning with the first one 29 years ago (FDA 1978). FDA's delay in finalizing the monograph and enforcing its provisions has spurred nine class-action, false-advertising lawsuits (Joseph Goldstein v. Schering-Plough Corporation, et al., 2006); a state Attorneys General petition requesting the Agency to set standards (Blumenthal 2006); a Congressional mandate for FDA to finalize the document (HR 2744, 2005); and at least two subsequent written requests from seven Senators urging the Agency to finalize the monograph in order to protect the public from skin cancer (Dodd 2007, Kerry 2007). EWG's research reveals serious deficiencies in the safety and efficacy of sunscreen sold in the U.S., deficiencies that have continued as a result of FDA's delay in finalizing the standards contained in the monograph (EWG 2007a).

Therefore, while we are pleased that FDA has issued amendments to the sunscreen monograph, FDA must strengthen and finalize the monograph, then strictly enforce its provisions so that consumers will be protected from ineffective and unsafe sunscreens currently on the market.

EWG's research shows that FDA's finalization of a strong monograph is critical. We found that some sunscreens on the U.S. market:

- offer inadequate protection from the sun;
- may be less safe and effective than products offered in other countries;
- are labeled with misleading product claims;
- contain ingredients with significant safety concerns.

Specifically, our research indicates that 83% of 868 sunscreen products offer inadequate protection from the sun, or contain ingredients with significant safety concerns. We found that only 17% of the products on the market are both safe and effective, blocking both UVA and UVB radiation, remaining stable in sunlight, and containing few if any ingredients with significant known or suspected health hazards.

The proposed, amended final monograph will begin to resolve these concerns, but significant gaps will remain. EWG is pleased that FDA has proposed standards that include a UVA rating system, sunburn protection factor (SPF) testing protocols, and provisions to help ensure that

sunscreen products remain effective when exposed to the sun (photostability). To ensure that a wide range of safe and effective sunscreens are available for consumers, we recommend the following improvements to the monograph and other FDA actions:

- **FDA should finalize the proposed amendments and sunscreen monograph within 3 months**, require rapid implementation by manufacturers, and then diligently enforce the monograph's provisions that help ensure the safety and efficacy of sunscreens. We recommend that FDA require full implementation of the monograph provisions within one year. These standards have been in development for nearly 30 years, and any further delay by FDA will result in additional, serious health impacts for consumers.

- **FDA must improve provisions for sunscreen effectiveness, including UVA and UVB protection and photostability.**
    - **UVA protection:** FDA should require at least a minimum level of UVA protection in sunscreen. The proposed amendments would allow products providing no UVA protection whatsoever to be classified as sunscreen. FDA should develop a health-based UVA rating system. The proposed system relies on measurements not directly related to health.
    - **UVB protection:** FDA should revise the monograph as necessary to protect consumers from the use of anti-inflammatories in sunscreens that can artificially boost SPF ratings.
    - **Photostability:** FDA should require manufacturers to identify and ensure the safety of all degradation products of sunscreens, and should require pre-irradiation tests that mimic real-world conditions and do not artificially inflate estimates of sunscreen effectiveness.

- **FDA should review pending sunscreen applications to provide manufacturers and consumers with access to a wide range of safe and effective sunscreens.** Safe and effective sunscreens in widespread use in other parts of the world are not yet approved for use in the U.S. because of FDA's continuing delay on reviews and approvals of new sunscreen ingredients.

- **FDA must improve and then enforce restrictions on misleading product claims.** EWG's research shows that at least 52% of products on the market bear claims that are considered unacceptable or misleading under the existing monograph or proposed amendments. FDA should address additional misleading claims in the monograph, including "chemical-free," "non-chemical," and "PABA-free."

- **FDA should ensure that all sunscreens are safe.**

    - **Safety standard:** FDA should require complete safety data for new sunscreens, approving sunscreens only if manufacturers can show that they are safe for vulnerable populations such as pregnant women, children, and the elderly.
    - **Safety reviews:** FDA should review the safety of sunscreens currently approved for use for which new toxicity data has become available, including oxybenzone, Padimate-O, and nano-scale mineral sunscreens (zinc oxide and titanium dioxide).
    - **PABA:** FDA should no longer allow the use of PABA in sunscreen, given its links to allergic reactions and health concerns associated with the free radicals it releases in the presence of sunlight.

Our detailed comments and recommendations on how FDA must strengthen the proposed amendments to ensure that safe and effective sunscreens are widely available for consumers are below.

FDA's proposed amendments fail to ensure that sunscreens will adequately protect consumers from UV radiation hazards

UVA Protection
EWG's research shows that many sunscreens fail to provide adequate UVA protection. Fully 13% of high SPF sunscreens (SPF of at least 30) protect only from sunburn (UVB radiation), and do not contain ingredients known to protect from UVA radiation, which studies link to skin damage and aging, immune system problems, and skin cancer (EWG 2007a). UVA protection and a clear UVA rating system are vital for protecting consumers from the adverse health impacts of sun exposure.

FDA's proposed amendments would require a first-ever UVA rating system for consumers. EWG supports the proposed *in vivo/in vitro* approach for evaluating UVA protection. We support the use of the *in vitro* test based on the Boots Stars Method (Boots 2004) that relates the relative absorption of the UVA-I portion of the spectrum to the entire UV spectrum in order to reflect the breadth of UVA protection. We believe the star rating system will effectively communicate to consumers the level of UVA protection in a product. While FDA's proposal represents a major improvement and we support its finalization, it leaves gaps that must be filled.

First, the proposed UVA rating system is not derived from tests that measure health-based endpoints. Instead, it combines the results of *in vivo* testing (a test that measures persistent pigment darkening, or PPD) with an *in vitro* test that relates the ratio of long UVA wavelengths (340 - 400 nm) to the rest of the absorbance spectrum. In the Proposed Rule, FDA notes that there is "little consensus about the amount of UVA radiation protection required." Persistent pigment darkening, while indicative of UVA exposure (tanning), has not been related to an endpoint of concern such as cancer, wrinkling, or inflammation. Therefore, FDA's approach may not be based on the best indicators of suspected UVA-related effects like cancer and photoaging. In the Proposed Rule, FDA tentatively concludes that the available evidence fails to show that sunscreen use alone helps prevents skin cancer or premature skin aging (FDA 2007 p. 49079), and calls for additional data to better understand UV exposures and the role of sunscreens in prevention of disease disease (FDA 2007, p. 49089). *We recommend that FDA finalize the UVA rating system as proposed to ensure that consumers have UVA protection information as soon as possible, and develop a health-based UVA rating as necessary data become available.*

Secondly, the proposed amendments would not require that sunscreens protect consumers from UVA radiation. FDA requires that products provide at least a minimal amount of protection from UVB radiation (an SPF of 2, or double the protection of bare skin), but under the Proposed Rule, would not likewise require at least a minimal amount of UVA protection.

FDA concedes in their proposal that they "cannot conclude whether UVB or UVA radiation is more harmful to humans based on the scientific data collected to date. Therefore, FDA considers both UVB and UVA radiation protection equally important at this time because scientific data demonstrates that both have harmful effects on the skin." Yet instead of requiring UVA protection, FDA has proposed to allow sunscreens on the market that may provide no UVA protection whatsoever, bearing only a "No UVA protection" warning for

consumers. Given FDA's concerns about potential health effects linked to UVA radiation, *EWG recommends that FDA require all sunscreen products to offer at least minimal UVA protection*.

UVB Protection
EWG has learned that some sunscreens may contain ingredients that act as anti-inflammatory agents (Kreider 2007; Stanfield 2005). Such ingredients would artificially boost SPF ratings by minimizing inflammation visible as sunburn. Products containing anti-inflammatories could raise consumers' risks of non-sunburn effects such as cancer, as consumers would lose the indicator of health risk provided by visible sunburn.

In existing and proposed UVB test protocols (FDA 1999, 2007; Miller 2005), the SPF rating is determined solely by the erythemic (sunburn) response. There are no provisions in either the Final Monograph or the Proposed Rule testing protocols for ascertaining other effects, such as formation of necrotic keratinocytes (Nelson 2005), that would not be masked by anti-inflammatory ingredients.

EWG recommends that FDA investigate the prevalence and influence of anti-inflammatory ingredients in sunscreen, and update UVB standards as necessary. If necessary, we recommend that FDA revise the monograph, expanding SPF protocols to require an *in vitro* measurement confirming the SPF rating based on UV transmission; require observations on SPF test subjects to determine whether UV radiation exposure has caused a non-erythemic (non-sunburn) effect; or otherwise establish limits on the extent to which non-active ingredients (base formulation) can contribute to efficacy ratings.

Photostability
EWG's research shows that 53% of products on the market contain ingredients that may be unstable alone or in combination (EWG 2007a). A number of studies identify ingredients and formulations that lose effectiveness in filtering out UV radiation or form potentially toxic degradation by-products over the course of normal exposure (Berset 1996; Bonda 2005; Chatelain 2001; Deflandre 1988; Gaspar 2006; Herzog 2002; Sayre 1999a; Sayre 1999b; Scalia 1999; Serpone 2002).

FDA's proposed amendments include new provisions to help ensure that sunscreens are adequately photostable to remain effective over typical periods of exposure. FDA's proposed amendments require pre-irradiation of sunscreen prior to *in vitro* UVA testing. The required *in vivo* SPF testing method inherently accounts for effects of photostability, with exposure durations comparable to consumers' typical outdoor exposures. Certainly photostability is necessary in products intended to protect consumers from sun hazards. FDA's new provisions for photostability are an improvement, but they are inadequate.

First, while UVB and UVA testing protocols account for photodegradation, FDA fails to require that manufacturers ensure the safety of chemical degradation products, some of which are inherently toxic and may pose an unreasonable risk to health. Numerous studies suggest that sunscreens lose effectiveness over the course of UV exposure (e.g., Bonda 2005 and EWG 2007a for UVB filters), through both photophysical and photochemical deactivation processes (Martincigh 1997). Some studies demonstrate a loss of effectiveness via photophysical deactivation processes (Bonda 2005), while other studies suggest that loss of effectiveness results from chemical breakdown that may result in the formation of harmful degradates (Damiani 2007; Martincigh 1997; Scalia 1999). *We recommend that FDA require manufacturers to identify and publicly document all degradation products of sunscreens, and require that all identified degradates meet all safety requirements for cosmetics and over-the-counter drugs.*

Second, the pre-irradiation FDA has proposed for UVA testing is not sufficient. It requires that products be pre-irradiated with UVA radiation only, even though the effectiveness of UVA filters could be compromised by exposure to other forms of radiation as well. For instance, the well-documented interactions between octyl methoxycinnamate (UVB absorber) and avobenzone (UVA absorber) can compromise the effectiveness of sunscreen products and may be driven by UVB exposures (Bonda 2005). *EWG recommends that FDA require pre-irradiation in ranges that simulate actual sunlight, as a consumer will experience outdoors*.

Lastly, the pre-irradiation tests are proposed in FDA's amendments to be conducted on glass plates, which may not accurately simulate how sunscreen ingredients react on the skin, as noted by FDA. *Again, EWG recommends that FDA improve pre-irradiation tests to reflect actual conditions for the consumer in future updates of the monograph*.

FDA has failed to conduct timely reviews of new, proposed sunscreens, leaving consumers with fewer options for sun protection than are available in other countries.
FDA has approved just 17 sunscreen chemicals for use in the U.S. At least 29 are approved for use in the E.U. FDA has approved only four chemicals effective in the UVA range for use in the U.S., and has failed to approve new, more effective UVA filters available in the E.U. and Asia. Effective sunscreens not approved in this country are in widespread use elsewhere in the world.

Some sunscreens proposed for use in the U.S. have been under review at FDA for over a decade. Some of the actives approved for use in the E.U. but not the U.S. were specifically designed to address concerns with the sunscreens currently in use in the U.S. Two sunscreens currently under FDA review, bisoctrizole and bemotrizinol, provide broad spectrum protection, are inherently photostable, and are not absorbed through intact skin (Herzog 2005). FDA sorely needs to streamline and modernize its sunscreen review process to give consumers access to the best products possible.

When FDA issued the final monograph (FDA 1999) for sunscreens (which was subsequently stayed indefinitely at the request of industry), multiple petitioners urged FDA to review active ingredients approved for use in Europe. The Agency replied it would "address sunscreen active ingredients that have foreign marketing experience and data at a future time." FDA has previously solicited comments on Isoamyl P-Methoxycinnamate, 4-Methylbenzylidene Camphor, Ethylhexyl triazone, Diethylhexyl Butamido Triazone, Bisoctrizole, and Bemotrizinol (FDA 2003, 2005, 2006). In the current proposed rule the Agency has approved new combinations of avobenzone with ensulizole and avobenzone with zinc oxide. But the proposed amendment contains no new, proposed active ingredients.

Because the Agency has failed to conduct timely reviews for new sunscreens, manufacturers are using unapproved sunscreens in products, but listing them as inactive ingredients, presumably to provide additional UV protection for consumers while still satisfying federal requirements. EWG's research found at least four sunscreen chemicals not approved for use in the U.S. listed as inactive ingredients in sunscreen products (Tinsosorb S, Drometrizole Trisiloxane, 4-Methylbenzylidene camphor (4-MBC), and Polysilicone-15). Notably, for one of these four chemicals (4-MBC), the European Union's Scientific Committee on Consumer Products recently was unable to verify its safety for use in sunscreen (SCCP 2006a).

EWG recommends that FDA streamline its Over-the-Counter (OTC) review process to quickly provide manufacturers and consumers with access to a wide range of safe and effective sunscreens. EWG also recommends that FDA limit the extent to which the base formulation of a product (inactive ingredients) can contribute to UVA and UVB effectiveness ratings.

FDA's proposed amendments fail to prohibit key, misleading product claims.
EWG's research shows that at least 52% of products on the market bear claims that are considered unacceptable or misleading under the existing monograph or proposed amendments (EWG 2007a). Our analysis of marketing claims on hundreds of sunscreen bottles shows that false and misleading marketing claims are common. Claims like "all day protection," "mild as water," and "blocks all harmful rays" are not true, yet are found on bottles.

EWG fully supports FDA's approach detailed in the Proposed Rule controlling product efficacy and health benefit claims, including protocols for determining water resistance and protection against photo-aging, cancer, wrinkling, etc. Further, we are pleased that confusing terms such as "shields from," "filters," "screens out," "reflects," "sunblock," "sun's rays," "sun's harsh rays," "sun's harmful rays," "burning rays," "8-hour," and "all day protection" will be prohibited on labels when FDA finalizes the Monograph and Proposed Rule. We found these terms used on the labeling of 330 products in our database.

We are concerned that neither the Final Monograph nor Proposed Rule takes a definitive position on restricting terms such as "chemical-free" and "non-chemical." We found these terms on 28 products in our database, although FDA has indicated that they view their use as probably unacceptable. We remain concerned that FDA will continue to sanction "PABA-free" claims on labeling, although we have not been able to identify a single sunscreen product containing PABA (p-aminobenzoic acid). At the current time, it appears to be an empty claim (one product even contains the term in its name) that misleads consumers into thinking the product is better or safer than other available sunscreens.

Therefore, in addition to the proposed provisions, *EWG recommends that FDA restrict the use of three additional terms that mislead consumers, "chemical-free," "non-chemical," and "PABA-free."*

FDA's proposed amendments fail to address sunscreens that pose significant safety concerns.
EWG research has identified a number of significant gaps in the publicly available toxicity data for sunscreen active ingredients, as well as a number of significant safety concerns indicated from the studies that are available. For example, studies raise concerns with respect to the safety of PABA, oxybenzone, Padimate-O, and nano-scale mineral sunscreens (zinc oxide and titanium dioxide) in sunscreen products. We have identified research pointing to allergenic responses, endocrine disruption, production of reaction oxygen species, absorption into the body, and environmental concerns for these ingredients (EWG 2007a).

EWG has compiled comprehensive hazard and regulatory information for all 17 active ingredients approved in the United States, as well as partial information on 31 actives approved elsewhere. We have found that aggregate exposures to ingredients may be more harmful to humans, especially vulnerable sub-populations such as a fetus, than is indicated by the Cosmetic Ingredient Review panel (EWG, 2004; EWG, 2005; EWG, 2007a).

The Proposed Rule identifies two new active ingredient combinations (avobenzone with zinc oxide and avobenzone with ensulizole) for approval as safe and effective in OTC formulations. While review of other active ingredient monographs is beyond the scope of the current monograph, EWG would like to highlight some of the data gaps and safety concerns with existing sunscreen actives.

The widespread concerns with PABA are such that hundreds of sunscreen products claim "PABA-free" on their labels. Even so, we found that no sunscreen product sold in the U.S. contains the ingredient. EWG recommends that FDA no longer allow the use of PABA as an active ingredient in sunscreen. PABA has been out of favor with sunscreen manufacturers, not only because of formulation difficulties, but also because of health concerns, including allergic reactions (Shaath 2005).

EWG recommends that FDA re-review the usage of Oxybenzone (Benzophenone-3) as an active sunscreen ingredient due to safety and environmental concerns. It recently underwent a re-review by the European Union's Scientific Committee on Consumer Products which found insufficient data to verify the required margin of safety (SCCP 2006b). Further, the SCCP panel noted that, "In the case of Benzophenone-3, the presented publications clearly indicate that the UV-filter is a photoallergen." The literature on reactive oxygen species (ROS) generation using oxybenzone is mixed; two of three studies indicate excess ROS (Allen 1996; Hanson 2006; Serpone 2002). Several studies have found this ingredient to be a weak endocrine disruptor by itself (Kunz, Galicia 2006; Ma 2003; Nakagawa 2002; Schlenk 2005; Schlumpf 2001; Schlumpf 2004) and in combination with other chemicals (Heneweer 2005; Kunz and Fent 2006), which may have both human health and environmental implications.

EWG also recommends a re-review for Padimate-O, based on ongoing health and efficacy concerns. Several studies have documented Padimate-O's ability to generate ROS when exposed to UV radiation (Allen 1996; McHugh 1997). Additionally, Padimate-O has demonstrated estrogenic activity *in vitro and in vivo* (Gomez 2005; Kunz and Fent 2006; Kunz, Galicia 2006; Schlumpf 2001) having implications for wildlife and potentially people. Several research groups found it to increase DNA strand breaks (Gulston 1999; Knowland 1993; McHugh 1997). Researchers have reported several types of allergic reactions to Padimate-O (Thune 1984; Weller 1984). Lastly, there is some indication of its photoinstability (Deflandre 1988; Scalia 1999; Serpone 2002), including one study in which Padimate-O, in combination with Avobenzone, lost 80% of its average monochromatic protection factor after only two minimal erythemal doses (Sayre R 1999).

EWG has commented to the Agency before on the use of nano-scale materials in personal care products (EWG 2006). The proposed amendment does not address nano-scale materials other than to approve new combinations of zinc oxide and avobenzone. We believe the Agency has a responsibly to review not only the use of nano-scale materials in cosmetics in general, but also to specifically review the use of nano-scale forms of titanium dioxide and zinc oxide in sunscreen products. EWG believes the Agency needs to establish their safety for use in sunscreens beyond the limited studies that were used during the initial approval process, including but not limited to coatings in order to reduce generation of reaction oxygen species and minimum particle sizes. Further, EWG recommends that FDA require that manufacturers publicly report particle size distributions or standardized grades. The toxicity of these ingredients has been reviewed by several parties, including EWG, and their overall safety has not been conclusively determined (CTFA 2006; EWG 2006, 2007a; ICTA 2006a, b; Nohynek 2007; Oberdorster 2005; SCCNFP 2000, 2003; SCCP 2005; EWG 2007b). The major concerns with these particles fall into one of several categories: cytotoxicity (Brunner 2006; Long 2006), reactive oxygen species generation (SCCNFP 2000; Uchino 2002) photoclastogenicity (Dufour 2006; SCCNFP 2003), skin penetration (Cross 2007; Gamer 2006; Gottbrath 2003; Mavon 2007), and ecotoxicity (Adams 2006). While our research indicates that these ingredients are photostable and effective across the entire UV spectrum, the human health and ecotoxicity concerns persist.

With respect to ingredient safety, we recommend that:

- *FDA require complete safety data for new sunscreens, approving sunscreens only if manufacturers can show that they are safe for vulnerable populations such as pregnant women, children, and the elderly;*
- *FDA review the safety of sunscreens currently approved for use for which new toxicity data have become available, including oxybenzone, Padimate-O, and nano-scale mineral sunscreens (zinc oxide and titanium dioxide);*
- *FDA no longer allow the use of PABA in sunscreen, given its links to allergic reactions and health concerns associated with the free radicals it releases in the presence of sunlight.*

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