Beyond Pesticides appreciates the prudent contemplation of insect repellent-sunscreen combination products EPA proposed in the reregistration eligibility decision (RED) for N,N-diethyl-meta-toluamide (DEET). We also appreciate this opportunity to share our concerns over these products. Beyond Pesticides interest in this issue lies in our effort to restrict pesticide use in a manner that protects public health and the environment, and to advance alternatives that eliminate dependency on toxic chemicals.

We oppose the reregistration of all DEET-sunscreen combination products for the following reasons:

1. **DEET exposure can result in negative health effects.** As the agency notes, the registration of DEET is unusual in that it is one of few residential-use pesticides that is applied directly to the skin. The result is that the public is being exposed to a pesticide that has the ability to cause in lab animals increased fetal loss, bone and skeleton abnormalities in the offspring of rabbits, birth defects in birds, reduction in size of the testes and degeneration, and has produced abnormal sperm with reduced motility. Additionally, the public is directly applying a chemical to their skin that is demonstrated to cross the placenta and move into fetal blood in humans, has the ability to cause mutagenicity and oxidative stress, can decrease sensory and motor skills, causes skin irritation and kills brain cells.¹

2. **Sunscreen exposure can result in negative health effects.** Sunscreen products typically contain several active ingredients and a slew of “inactive” ingredients. Parabens and fragrance are commonly included, among other chemicals of concern. Common sunscreen brands include ingredients that are irritants, endocrine disruptors, carcinogens, are neurotoxic, immunotoxic, etc., in their products.²

3. **Combination products encourage increased DEET exposure.** As the agency points out, DEET is widely used among the U.S. population (27% of adult males, 31% of adult females and 34% of children). So is sunscreen. DEET products are intended for spare, infrequent use. Sunscreen is intended for liberal, frequent use, and is often used in situations where an insect repellent is not needed. This creates not only a labeling nightmare, but leads to multiple applications of repellent-sunscreen products, increasing the risk of health effects – a reasoning which has led Health Canada to conclude in 2002 “The combination [DEET+sunscreen] products should be discontinued.”

EPA lists DEET-sunscreen combination products as containing 7.13-20% active ingredient DEET. Continuing to allow DEET-sunscreen combination products will increase unnecessary exposure to DEET, likely on a widespread scale, including pregnant women and children.

4. **Label compliance is not feasible, negating vital risk mitigation efforts.** Upon Health Canada’s decision on the same issue, they considered “that use of these products could lead to an overapplication of DEET due to the discordant use instructions (i.e., sunscreens should be applied liberally and frequently to maximize protection from the sun, but insect repellents such as DEET should be applied only sparingly and infrequently).”

EPA's failure to include the lack of or limited compliance with label restrictions in its risk assessment of the chemical results in inadequate protection of the public’s, including children’s, health. Sunscreen directions and use patterns do not correspond with the label requirements EPA imposed for DEET (RED), specifically:

   a. EPA’s RED states, “Some DEET formulations have label language and/or brand names that imply that those formulations are better for use on children (e.g. “…for children,” “…for kids.”) The Agency considers these formulations/products to be ineligible for reregistration.” This decision automatically requires that DEET never be formulated with sunscreen products that make similar child-safety claims.

   b. “Do not apply over cuts, wounds, or irritated skin.” Anyone who burns and/or peels and is repetitively outdoors will be reapplying sunscreen products to irritated skin.

   c. “Do not apply near eyes and mouth. Apply sparingly around ears.” It is not unusual for sunscreen users to apply liberally on the face and around

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4 Health Canada (2002)
the ears. As most of us know, regardless if a sunscreen claims to be water and/or sweat resistant or not, it often ends up in the eyes and mouth during activities that involve water or strenuous activity. Sunscreens also often transfer onto other things we come into contact with, such as towels, food, etc.

d. “Do not apply to children’s hands.” Parents often cover at least the top of their children’s hands with sunscreen.

e. “Use just enough repellent to cover exposed skin and/or clothing.” Consumers, especially those prone to burns, often put on several coats to avoid uneven coverage.

f. “Do not use under clothing.” People often apply sunscreen for the lightest layer of clothing they plan on wearing (e.g. bathing suit, etc.) and then layer clothes on top.

g. “Avoid over-application of this product.” This phrase particularly contradicts typical sunscreen directions. Sunscreen labels call for liberal and frequent applications.

5. **Potential for synergistic effects.** There is a history of concerning synergistic effects regarding DEET mixtures. It has been established that in combination with ethanol, a common solvent used in DEET products (and sunscreen), the amount of DEET absorbed through the skin increases. Synergistic effects of DEET and permethrin have been documented to include a decrease in the permeability of the blood-brain barrier, impairment of sensorimotor performance, decreased activity of acetylcholinesterase, behavioral changes, increased damage to DNA, reduction in the ability of the liver to break down either chemical, and increased cell death. Synergistic effects of DEET and malathion have also been observed to increase nerve cell death in the midbrain. In combination with chlorpyrifos, DEET increases the transformation of the chemical to chlorpyrifos-oxon, a potent nerve poison. Going beyond the laboratory in 1987, the flea and tick spray HartzBlockade (8.5% DEET, 0.45% fenvalerate) caused a rash of pet poisonings and deaths.

There are also a number of studies that have documented some basic synergistic effects resulting from the combination of pesticides and sunscreens, including:

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6 Cox, C (2005)
7 Beyond Pesticides (2002)
a. A 2003 study by Brand et al., building off of previous work that had established “dermal penetration of the herbicide 2,4-D can be enhanced by commercial formulations containing chemical ultraviolet (UV) absorbers, the absorbers themselves and the insect repellent DEET,” looked at the interaction between sunscreens containing titanium dioxide or zinc oxide and the pesticides 2,4-D, paraquat, parathion and malathion using hairless mouse skin. The data revealed, “pretreatment with five of the nine sunscreens [depending on formulation] tested increased the transdermal absorption of 2,4-D (P<0.05). Transdermal studies using paraquat, parathion and malathion pretreated with a representative sunscreen all demonstrated significant penetration enhancement when compared to controls (P<0.05).”

Further work by Brand et al., published in 2007, states “Both alcohol consumption and topical sunscreen application act as transdermal penetration enhancers for model xenobiotics.” Using skin from rats, the study focuses on 2,4-D absorption. “Comparing 2,4-D transdermal absorption after exposure to both ethanol and sunscreen with a theoretical value (sum of penetration after ethanol or sunscreen treatment) demonstrates that these two treatments enhance additively at the higher doses tested.”

Both of these studies offer a glimpse of the larger potential for synergistic effects of repellent-sunscreen combination products with other substances, such as other pesticides, of which simultaneous exposure is a likely common real world scenario.

b. In 2005, Gu et al. looked at the interaction between DEET and the sunscreen active ingredient oxybenzone (present in Coppertone, Neutrogena, Bain de Soleil, etc., including products marketed specifically for babies and children), including combined repellent/sunscreen lotions, on piglet skin. The researchers concluded, “Concurrent application of commercially available repellent and sunscreen products resulted in significant synergistic percutaneous permeation of the repellent DEET and the sunscreen oxybenzone in vitro.”

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11 EWG (2007)
A 2007 study by Wang and Gu\textsuperscript{12} looked at DEET and oxybenzone again, this time using human skin. They found “DEET permeated transdermally more across human skin than oxybenzone, and both compounds acted as permeation enhancers when used simultaneously. Premixing repellent and sunscreen enhanced the overall penetration of both DEET and oxybenzone.”

c. A study conducted by Murphy et al. (2000)\textsuperscript{13} grew out of previous work that revealed “Sunscreen loses efficacy when used with the insect repellent N,N-diethyl-3-methylbenzamide (diethyltoluamide; deet). A previous study demonstrated a 33.3\% decrease in sun protection factor when insect repellent and sunscreen were applied sequentially to the skin.” After observing efficacy in a series of test groups using different combinations of sunscreen and insect repellent, “The results of this study showed that insect repellent has the same efficacy even when sunscreen is applied with it.”

These results suggest the efficacy of sunscreen may be reduced by DEET in the products being considered for reregistration, which would further justify the agency’s concern over unnecessary DEET exposure via repellent-sunscreen combination products, as consumers would need to reply the product more often.

d. Ross et al. (2004)\textsuperscript{14} also looked at the combination of DEET and sunscreen to test for synergistic effects using hairless mouse skin. The researchers “confirmed substantial penetration of a 20\% DEET standard. Despite a lower (10\%) DEET content, a commercially marketed sunscreen formulation had a 6-fold more rapid detection (5 versus 30 min) and 3.4-fold greater penetration at steady state.”

6. \textit{Children are frequently exposed to DEET products and are particularly susceptible to health effects.} As it has been establish, over a third of the nation’s children have been purposely exposed to DEET; it is also common knowledge that sunscreen use is widespread in the nation’s population, including children, for whom separate product lines have been developed. As the agency also knows, children take in more pesticides relative to body weight than adults and have developing organ systems that are more vulnerable and less able to detoxify toxic chemicals. Regardless of the agency’s decision that there is insufficient data, the reports suggesting DEET use and seizures among children are connected, and the

high potential for known and unknown synergistic effects require a precautionary approach.

7. Alternatives to DEET are available. The U.S. Centers for Disease Control and Prevention recommends oil of lemon eucalyptus and picaridin as good alternatives to DEET, providing a comparable protection.\(^\text{15}\) Other alternatives include essential oils and citronella sprays. Even with these active ingredients the agency would need to ensure that use restrictions do not countervail sunscreen use instructions.

In light of the above points, Beyond Pesticides asks the agency to follow the lead of the Canadian government and deny reregistration of all DEET-sunscreen combination products. We also ask the agency to conduct a thorough review of synergistic effects when considering any repellent-sunscreen combination product. Beyond Pesticides appreciates the agency’s consideration of the above comments.

Sincerely,

Laura Hepting  
Special Projects Coordinator  
Beyond Pesticides

\(^{15}\) CDC. 2005. CDC Adopts New Repellent Guidance for Upcoming Mosquito Season.  
http://www.cdc.gov/od/oc/media/pressrel/r050428.htm