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November 17, 2000

The Honorable Carol Browner
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on Test Plan for Irganox 1076 (Octadecyl 3,5-di(tert)-butyl-4-hydroxyhydrocinnamate)

Dear Administrator Browner:

The following comments on the test plan for Irganox 1076 (Octadecyl 3,5-di(tert)-butyl-4-hydroxyhydrocinnamate) are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These animal protection and environmental organizations have a combined membership of more than nine million Americans.

The summary submitted by Ciba Specialty Chemicals Corporation appropriately does not call for any additional testing on this well-characterized chemical. The data provided are more than adequate under High Production Volume (HPV) Program guidelines. However, the presentation of the test plan raises some questions regarding compliance with the original HPV framework agreement in which sponsors committed to performing a thorough review of existing data. These concerns include:

- The summary presents minimal data and little discussion of its ability to meet the HPV standards and obviate the need for more tests. No qualitative information on the compound's application and behavior is provided.
- Ciba failed to identify additional existing information on Irganox 1076, as several studies in the scientific literature and government databases describe the toxicity, fate, and transport of this chemical.
- This compound is already registered as an FDA food contact substance and more toxicological information may be available. Accordingly, we have submitted a Freedom of Information Act (FOIA) request for this information.
- The lack of description of the compound's use, structure, and behavior limits the ability to use the presented data in the development of chemical categories. At minimum, Irganox 1076 could be grouped with the similar compound presented by Ciba, Irganox 1010 (Tetrakis-(methylene-(3,5-ditertbutyl-4-hydrocinnamate)methane).

The EPA needs to play a strong role in requiring that companies perform a thorough review of the literature and present all available information on the proposed chemicals. The EPA also needs to assume a stronger

role in promoting cooperation among participants with respect to chemical category formation. We ask the EPA to inform us how it intends to foster this cooperation in the development of chemical categories so that unnecessary, expensive, and poorly conceived testing is avoided. While Ciba does not call for additional testing, we are concerned that a regulatory review may disagree with Ciba's claim that no further tests are necessary. We believe that additional testing of this well-understood compound would be redundant and would not contribute to a greater understanding of the public health impact of Irganox 1076. It should be noted that in the event additional testing is called for, the testing must be deferred until November 2001 or later, as Irganox 1076 is an individual chemical.

I can be reached via telephone at 202-686-2210, ext. 302, or via e-mail at <ncardello@pcrm.org>. Correspondence should be sent to my attention at the following address: PCRM, 5100 Wisconsin Ave., Suite 404, Washington, DC 20016. I look forward to your response on this important issue.

Sincerely,

Nicole Cardello, MHS
Research Coordinator

cc: The Honorable Robert C. Smith
The Honorable F. James Sensenbrenner, Jr.
The Honorable Ken Calvert
The Honorable Jerry Costello
Council on Environmental Quality

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General Comments on the Test Plan for Irganox 1076

The Ciba Specialty Chemicals Corporation has provided available in-house study results on Irganox 1076 that address each health endpoint of the SIDS battery and therefore appropriately has not called for more tests. However, the summary does raise some concern regarding the original HPV framework agreement in which sponsors committed to conducting a comprehensive review of existing data. We are providing further justification for Ciba's contention that no additional tests are needed under HPV guidelines.

Irganox 1076 is a sterically hindered phenolic antioxidant used as a stabilizer for organic substrates such as plastics. Irganox 1076 is a large, high molecular weight (MW= 530.873 g/mol), hydrophobic compound with low volatility. These physicochemical properties most likely explain the relatively low toxicity of Irganox 1076 on animals used in laboratory tests. No major toxic effects were seen, even at doses exceeding EPA limit doses. For example, the oral LD-50 was found to be greater than 5000 mg/kg bodyweight, the dermal LD-50 was found to be greater than 2000 mg/kg bodyweight, and no mutagenicity was observed. This chemical has been tested on many animals and any further testing on animals would not contribute to the understanding of its toxicity.

Several studies in the scientific literature provide additional information on the toxicity, fate, and transport of Irganox 1076 (see Table 1). Inclusion of results from these studies would provide a more comprehensive understanding of the properties and behavior of the compound.

Other Existing Toxicity Studies

As presented in Table 1, a literature review of Irganox revealed that an additional mutagenicity assay was conducted by Yoshida,[1] and no mutagenicity was observed. Lake *et al*.[2] studied the induction of xenobiotic metabolism by Irganox 1076.

Environmental Fate and Transport Studies

As presented in Table 1, studies by Fisher *et al*.[3] and Herrchen *et al*.[4] explore the environmental fate and transport of Irganox 1076 and present results that may enhance the theoretical fugacity calculations presented in Ciba's summary. The mobility of antioxidant additives from food-packaging material has recently become a subject of interest. Several studies examine the fate and transport of Irganox 1076 from food-packaging substances. These studies explore many factors affecting migration, environmental fate and transport, and potential exposure scenarios.[5-8]

Chemical Categories

Ciba failed to compare Irganox 1076 with other similar chemicals to form a group of phenolic compounds. Chemical categories should be formed whenever possible to reduce testing of other similar compounds.

Irganox 1076 is one of many hindered phenolic stabilizers and could easily be grouped with another chemical proposed by Ciba, Irganox 1010 (tetrakis-(methylene-(3,5-di-tertbutyl-4-hydrocinnamate)methane. We ask the EPA to inform us how it intends to foster cooperation in category development so that unnecessary, expensive, and poorly conceived testing is avoided.

Conclusion

Although Ciba Specialty Chemicals Corporation has presented its in-house data and appropriately not called for any testing, interpretation of study results and a comprehensive review of existing data are needed to provide a complete summary of the chemical's properties, behavior, and toxicity. Additionally, the inclusion of Irganox 1076 into a chemical category should be considered.

References

1. Yoshida Y. Mutagenicity of photoreaction products of 2,6-di-tert-butyl-4-methyl-4-tert-butylperoxy-2, 5-cyclohexadienone and of photoreaction products of octadecyl 3-(1-tert-butylperoxy-3, 5-di-tert-butyl-4-oxo-cyclohexa-2, 5-dien-1-yl)proprionate. Osaka-Furitsu Koshu Eisei Kenkyusho Kenkyu Hokoku Shokuhin Eisei Hen 1981;12:95.
2. Lake BG, Gangolli SD, Schmid K, Schweizer W, Staubli W, Waechter F. The induction of rat hepatic microsomal xenobiotic metabolism by n-octadecyl beta-(3',5'-butyl-4'-hydroxyphenyl)-proprionate. Food Cosmet Toxicol 1980;18(1):47-54.
3. Fisher K, Norman S, Freitage D. Studies of the behaviour and fate of the polymer-additives octadecyl-3-(3,5-di-t-butyl-4-hydroxyphenyl)propionate and tri-(2,4-di-t-butylphenyl) phosphite in the environment. Chemosphere 1999;39(4):611-25.
4. Herrchen M, Kordel W, Klein W. Assessment of the environmental behaviour of antioxidants in folios. Comparative risk analysis of the use of folios in agriculture. Chemosphere 1997;35(11):2627-44.
5. Garde JA, Catala R, Gavara R. Global and specific migration of antioxidants from polypropylene films into food simulants. J Food Prot 1998;61(8):1000-6.
6. Limm W, Hollifield HC. Effects of temperature and mixing on polymer adjuvant migration to corn oil and water. Food Addit Contam 1995;12(4):609-24.
7. Cooper I, Goodson A, O'Brien A. Specific migration testing with alternative fatty food simulants. Food Addit Contam 1998;15(1):72-8.
8. Bieber WD, Frytag W, Figge K, vom Bruck CG, Rossi L. Transfer of additives from plastics materials into foodstuffs and into food simulants–a comparison. Food Chem Toxicol 1984;22(9):737-42.

Table 1. Literature Review of Irganox 1076

Author	Title	Source	Subject
Yoshida, 1981	Mutagenicity of Photoreaction Products of 2,6-di-tert-butyl-4-methyl-4-ter-butylperoxy-2, 5-cyclohexadienone and of photoreaction products of octadecyl 3-(1-tert-butylperoxy-3, 5-di-ter-butyl-4-oxo-cyclohexa-2, 5-dien-1-yl)proprionate.	Osaka-Furitsu Koshu Eisei Kenkyusho Kenkyu Hokoku Shokuhin Eisei Hen	mutagenicity
Lake *et al.,* 1980	The Induction of rat hepatic microsomal xenobiotic metabolism by n-octadecyl beta-(3',5'-butyl-4'-hydroxyphenyl)-proprionate	Food Cosmet Toxicol	metabolism/ toxicity
Fisher *et al.*, 1999	Studies of the behaviour and fate of the polymer-additives octadecyl-3-(3,5-di-t-butyl-4-hydroxyphenyl)propionate and tri-(2,4-di-t-butylphenyl phosphite in the environment.	Chemosphere	environmental fate and transport
Herrchen *et al.*, 1997	Assessment of the environmental behavior of antioxidants in folios	Chemosphere	environmental fate and transport
Garde *et al*., 1998	Global and specific migration of antioxidants from polypropylene films into food simulants	J Food Prot	fate/transport; migration to food substances
Limm *et al*., 1995	Effects of temperature and mixing on polymer adjuvant migration to corn oil and water	Food Addit Contam	fate/transport; migration to food substances
Cooper *et al*., 1998	Specific migration testing with alternative fatty food substances	Food Addit Contam	fate/transport; migration to food substances
Bieber *et al*., 1984	Transfer of additives from plastics materials into foodstuffs and food simulants–a comparison	Food Chem Toxicol	fate/transport; migration to food substances