



ESCO Company Limited Partnership

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December 5, 2003



201-14879

Mike Leavitt, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program

RE: EPA HPV Registration No.:

Dear Administrator Leavitt,

ESCO Company Limited Partnership is electronically submitting the enclosed revised test plan and revised robust summaries for the HPV Challenge Program, AR-201. The revised test plan and revised robust summaries are being submitted for the chemical category designated as the "color former" category. This color former category includes the following three chemicals:

Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3-one, 6'-(diethylamino)-3'-methyl-2'-(2,4-dimethylphenylamino)- (C.A.S. No. 36431-22-8),

Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 6'-(diethylamino)-3'-methyl-2'-(phenylamino)- (C.A.S. No. 29512-49-0), and

Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 6'-(dibutylamino)-3'-methyl-2'-(phenylamino)- (C.A.S. No. 89331-94-2).

This electronic submission includes this cover letter in Adobe Acrobat format (file name: Cover Letter for Color Former Submission-Revised.pdf), the revised color former robust summaries in Adobe Acrobat format (file name: Color Former Category Robust Summaries-Revised.pdf), and the revised color former test plan in Adobe Acrobat format (file name: Color Former Category Test Plan-Revised.pdf). Please post these revised submissions on the EPA HPV Challenge web site.

Included below is a summary of the comments that were received from the EPA on our test plan and robust summaries and our response to those comments.

Test Plan

Physicochemical Properties

Comment: *Boiling point.* In the robust summary, the submitter only indicates that these chemicals melt at temperatures above 168 °C, and that no boiling point data have been generated.

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Although measured boiling point data are needed for these chemicals, their high melting points suggest that these chemicals will boil or decompose at very high temperatures. According to OECD guidelines, if boiling points of chemicals exceed 300 °C, estimated values will be acceptable.

Response: Estimated boiling point data for each of the color formers in the category has been included in the robust summaries and in the test plan.

Environmental Fate

Comment: *Stability in water.* The submitter obtained the reported half-life values of 150, 150, and 60 days for Black XV, N-102, and ODB-2, respectively, from EPIWIN. EPA notes that these values are derived from the Level III model in EPIWIN from the BIOWIN estimates and are not related to hydrolysis. Although EPA agrees with the submitter that HYDROWIN v1.67 would not estimate a hydrolysis rate constant for this class of compounds, these chemicals contain a cyclic ester group that may be susceptible to hydrolysis. Therefore, the submitter needs to provide measured stability in water data for Black XV following OECD Guideline 111.

Response: The test plan and robust summaries for hydrolysis were revised to delete the half-life values from the BIOWIN estimates and adjusted to show that the HYDROWIN model could not estimate a hydrolysis rate. An ecotoxicity study on aquatic invertebrates contained information on the water stability of Black XV over time. A robust summary of the Black XV water stability information from this study was included and the test plan also now reflects the results from this information.

Comment: *Fugacity.* The submitter needs to include the input values used in the model in the fugacity robust summary.

Response: The fugacity robust summary has been revised to include the input values used in the model.

Health Effects

Comment: Although data are available for acute and genetic toxicity endpoints on all three compounds and the submitter's plan to use ODB-2 data to address data gaps on the repeated-dose, reproduction, and developmental toxicity endpoints is acceptable, the adequacy of these data can not be determined until the submitter provides critical information in robust summaries, specifically the purity of the tested substance.

Response: Each of the robust summaries has been revised to include the purity of the tested substance.

Comment: *Acute Toxicity.* The test plan matrix (Table 1) incorrectly indicated that an acute dermal toxicity study was available for N-102. No robust summary was submitted for this

compound, as correctly indicated in the Toxicological Data Table 5. The submitter needs to correct this discrepancy.

Response: The test plan matrix (Table 1) was revised to show that there is no acute dermal toxicity study available for N-102.

Comment: *Developmental Toxicity*. The submitter used a one-generation reproduction toxicity study on ODB-2 that includes pertinent developmental toxicity information to address the developmental toxicity data gap. The submitter needs to provide this information in a separate robust summary for this endpoint.

Response: A separate robust summary was developed for the developmental toxicity endpoint using the one-generation reproduction study on ODB-2.

Specific Comments on the Robust Summaries

Health Effects

Comment: *Acute Toxicity*. Black XV robust summaries need to include the results of body weight examination.

Response: The Black XV robust summary was revised to include the results of body weight examination.

Comment: *Repeated-Dose Toxicity*. A summary for the 28-day gavage assay of ODB-2 lacked the magnitude of the reduction in adrenal weights in high-dose females. The latter information is needed to evaluate the identification of 1000 mg/kg/day as a NOAEL.

Response: The robust summary for the 28-day gavage assay of ODB-2 was revised to include information on the magnitude of the reduction in adrenal weights in high-dose females.

Comment: *Genetic Toxicity*: Robust summaries for bacterial gene mutation assays need the following missing information: positive control data, the number of replicates, and the criteria for judging the results.

Response: The robust summaries for bacterial gene mutation assays were revised to include information on positive control data, the number of replicates, and the criteria for judging the results.

Comment: *Genetic Toxicity*: The summaries for *in vitro* chromosomal aberration assays for all three compounds lack the following information: culture harvest time, number of metaphases examined per concentration, cytotoxic concentration, positive controls, and criteria for determining positive results.

Response: The robust summaries for *in vitro* chromosomal aberration assays for all three compounds were revised to include the following information: culture harvest time, number of metaphases examined per concentration, cytotoxic concentration, positive controls, and criteria for determining positive results.

Comment: *Reproductive Toxicity*: All results of this study are provided as qualitative statements such as “similar to those of control animals.” The submitter needs to provide quantitative data in tabular form in order for EPA to assess the adequacy of these data. Also, if available, the submitter needs to provide the number of corpora lutea, whether or not histopathological evaluation of reproductive organs was conducted and the specific results of this evaluation.

Response: The robust summary for reproductive toxicity and developmental toxicity were revised to include quantitative results in tabular form from the one generation reproductive study.

Included below is a summary of the comments that were received from Environmental Defense on our test plan and robust summaries and our response to those comments.

Test Plan

Comment: These chemicals have a very low water solubility and tend to partition into the sediment where they have long half-lives. Because these properties indicate likely persistence of these chemicals in the environment, some discussion in the Test Plan of their synthesis, uses and transport that could result in possible release into the environment would be helpful.

Response: Color formers are sold to paper companies who produce carbonless and thermal paper. The color formers are coated on carbonless and thermal paper. Carbonless paper may be used for multicopy forms. Thermal paper may be used for point-of-service receipts. Color formers are a solid and are typically shipped in supersacks or paper bags by truck.

Robust Summary

Comment: Studies for toxicity to fish indicate the value for 100% mortality is the same as that for no mortality. We realize that no toxicity was observed, but these statements could be misleading or confusing to the public. We feel it would be better to state that no toxicity was observed.

Response: The robust summaries for toxicity to fish were revised to provide more clarity.

Comment: Studies in rainbow trout indicate significant potential for bioaccumulation and long half-life in fish. We realize these are not SIDS elements, but this work does raise an additional flag regarding the potential for negative effects should these chemicals be released into the environment.

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Response: Based on color former use and transport, it does not appear that there is significant likelihood of colorformers getting into waterways.

Included below is a summary of the comments that were received from Physicians Committee for Responsible Medicine (PCRM) on our test plan and robust summaries and our response to those comments.

Comment: PCRM is concerned that no further animal testing be conducted.

Response: ESCO Company does not anticipate that any further animal testing would be necessary.

If you have any questions, please call me at 231-727-6459 or my e-mail address is Bkatje@escocompany.com.

Sincerely,

Bruce Katje
Regulatory Compliance Manager

Attachments