UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Memorandum:

Subject: Secondary Reviews of: A) " Biodegradability of Dodecyl Dimethyl Amine Oxide (DDAO), B) Isolation, Identification and Quantitation of Semi-Continuous Activated Sludge Metabolite(s) of Dodecyldimethylamine Oxide, C) Biodegradation Study of E-5139.01 Continuous Activated Sludge Simulation Test and D) Fate of ^{14}C-Dimethyldodecylamine Oxide (DDAO) During Activated Sludge Treatment (CAS Test)."

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DP Barcode: D244071 Case type: Registration
Submission: S538885 CAS#: 68585-34-2
Chemical Name: Alkyl (C_{10-16}) Dimethylamine Oxide Common Name: (DDAO)
Commercial Name: Cleaning Magic I
MRID#s: 444349-14, 444349-15, 444752-05, 444752-06

Introduction:

The Proctor & Gamble Company has submitted environmental fate studies on biodegradation (studies listed here as A, B, C and D) of the product Cleaning Magic I to support the registration of this submission. Versar, a contractor of the Antimicrobials Division has performed the primary review and its conclusions and summaries are included in this report. N. Shamim of RASSB has performed the secondary review of the studies and additional conclusions and recommendations of RASSB are also included in this review package.

The registrants must note that for the proposed use of the product a as hard surface sanitizer, the Agency requires hydrolysis study (guideline #: 161-1) as part of environmental fate data requirements as this study will likely provide information about the stability (half life) of the product or/and formation of transformation products (degradates) of the parent substance.

Discussion:

P & G has submitted a proposed label for Cleaning Magic I which lists alkyl(C_{10-16}) dimethylamine oxide as the active ingredient (4.81%) and the label states that the product cleaning Magic I is " concentrated dishwashing detergent, antibacterial, and effective on grease." The CSF submitted by P & G, however, lists alkyl dimethylamine oxide twice- at one place it is listed as 4.32% (upper certified limits) and in the second place 3.79% (32%). These do not add up to 4.89% as claimed on the label.

A) A Biodegradability Study of Dodecyldimethylamine Oxide (MRID#: 444349-14)

Summary of the Submission:

1. This study was aimed at determining the amount of carbon dioxide evolved, to measuring the primary degradation and assessing the ultimate biodegradability and determining the amount of nitrogen present in the parent compound.

2. Primary degradation occurred at 97.5% within two days. The production of carbon dioxide reached a plateau at 63% evolution of carbon dioxide. The study indicates that some nitrogen containing intermediates (degradates) may be present.

3. BOD (Biochemical Oxygen Demand) was determined for the parent compound in 5 days and 20 days after the study commenced.

4. DBAS Method (disulfine blue active substance) was used to determine amount of the parent compound.

5. Primary degradation was measured by following the loss of DBAS and the

duration was 2 days for 97.5% degradation. In this time period 23.3% of the theoretical carbon dioxide was evolved and the evolution of carbon dioxide reached a plateau at 63.1% .

6. Only 50% nitrogen was determined by Kjeldahl method at the end of 26 days which indicated the presence of nitrogen containing degradates. These degradates were qualitatively recognized and not unequivocally identified by TLC or any other technique.

RASSB Conclusions & Recommendations:

1. The Risk Assessment & Science Support Branch has noted that this study (MRID#: 444349-14) was completed in January of 1977 at which time the GLP (or GALP) were not in place and the entire study was not conducted according to biodegradability guidelines (OPPTS Test Guidelines Series 835: Fate, Transport and Transformations). RASSB also notes that the biodegradability study was conducted on Dodecyl amine oxide in place of the actual active: alkyl (C_{10-16}) dimethyl amine oxide.

2. No QA/QC procedures were discussed in the study and the study was conducted for 26 days. OPPTS guidelines Series 835 require the study to be conducted for 28 days.

3. The study does not indicate the temperature and pH at which the data were collected.

4. Protocols for DBAS method were not provided with the study.

5. Sample calculations for the analytical results were not provided.

RASSB concludes that:

The study as submitted has many data gaps as well as the fact that the study was conducted more than twenty years ago. RASSB, therefore, recommends:

The study in the present format should be rejected and the registrants be asked to resubmit a new study which should be conducted according to the OPPTS guideline Series 835 with proper GLP and with attachment of relevant protocols.

B) Isolation, Identification and Quantitation of Semi-Continuous Activated Sludge Metabolite(s) of Dodecyldimethylamine oxide(DDAO) (MRID#: 444349-15)

Summary of the Submission:

1. Dodecyl dimethyl amine oxide, present in a semi-continuous activated sludge (at a nominal concentration of 10 ppm), was found to biodegrade under aerobic conditions within 24

hours (23 hours to be exact). The biodegradation was measured by the loss of DBAS. The same method was also employed to determine the initial concentration of the parent compound.

2. Radiolabeled study on the parent compound indicated the presence of radioactivity between 14.6 to 8.6% in the effluent. The identity of metabolites was investigated IR, ^{13}C nmr and mass spectrometry and only one metabolite was positively identified (dimethyl (4-hydroxybutyl)-amine-N-oxide). It was also noted that this metabolite is hygroscopic.

3. The metabolite isolation and identification was carried out by first freeze-drying the SCAS effluent liquid fraction, extracted (in methanol) and purified on Sephadex LH-20 and Partisil-10 PAC columns. The eluents were extracted in chloroform or ether. IR and mass spectrometry was performed after proper separation and sampling. Similarly, C-13 nmr study was conducted on the extracts collected. Quantitation of the metabolite was not possible as DDAO is hygroscopic.

RASSB's Conclusions and Recommendations:

1. Risk Assessment & Science Support Branch has noted that this study was conducted and completed in 1978 at which time the GLP or GALP were not in place nor were the biodegradability guidelines. RASSB also notes that the study was carried out on dodecyl dimethyl amine oxide and not on the active (alkyl (C_{10-16}) dimethyl amine oxide).

2. Experimental conditions for the activated sludge like pH, temperature and bacterial kinetics were not specified.

3. QA/QC procedures were outlined in the study (% recovery, precision, LOQ of the analytical instruments (HPLC, IR, mass spectrometer, LSC) and the mass balance data for the radiolabeled analysis.

4. Sample calculations for the data were not provided.

5. The metabolite and its analytical data provided are for the DDAO and not for the actual active (ADAO) in the product formulation. The Agency is not convinced that the same metabolite will be produced from the active under the same condition of the experiments.

RASSB concludes that the present study is unacceptable in the present form. If, however, the registrants can provide the following additional information, the Agency will give due consideration for acceptance of the study:

a. Reaction conditions, including the temperature and pH.

b. Sample calculations of the analytical data.

c. Running conditions and the make/year of the analytical instruments used (Ir, mass spec and C-13 nmr.)

C) Biodegradation Study of E-5139.01 Continuous Activated Sludge Simulation Test (MRID#:444752-05):

Summary of the Submission:

1. This study was conducted to measure the removal/biodegradability of a radiolabeled (^{14}C) dimethyldodecyl amine oxide using the SCAS Test Method. The protocols for the method are mentioned in the submission, but a copy of the protocols were not provided.

2. Two test units, containing the test substance along with the activated sludge made up of the synthetic and natural sewage, were investigated at a known test substance concentration.

3. The first of the two test units showed a removal of 88% of the test substance and the registrants estimated that the 76% was through biodegradation and 16% by sorption. Overall organic carbon removal was 93%. The percent removal for the second test unit was 79% and the registrants estimated that 69% of this was through biodegradation and 12% through sorption.

4. The COD (Chemical Oxygen Demand) of the influent was kept at a value between 260 mg/L to 430 mg/L.

5. The removal of the test substance was estimated through the measurement of radiolabeled $^{14}CO_2$. Liquid Scintillation Counting (LSC) was used to measure the radioactivity.

RASSB's Conclusions & Recommendations:

1. The COD value from the influent exceeded the protocols value of 260-430 mg/L.

2. The study temperature ranged from 15 ° C to 28 °C instead of the required range of 22± 2 °C.

3. During the study the pH was not kept constant.

4. The copies of SOPs were not provided with the submission by the registrants.

5. QA/QC procedures were also not provided with the submission.

6. Running conditions, make/year of the analytical instruments were not provided.

RASSB, concludes that the submission is scientifically not sound and that the variations of some of the parameters like mass of the influent, range of temperature, pH of the system would make the conclusions of the study unreliable and therefore, the study should be rejected and the registrants must submit a new study conducted according to the OPPTS guidelines 835.

D) Fate of ^{14}C-Dimethyldodecylamine Oxide During Activated Sludge Treatment (CAS Test). (MRID #: 444752-06)

Summary of the Submission:

1. The study was conducted for the purpose of determining the distribution of the active ingredient between the solid (sludge) phase as well as in the effluent (aqueous) phase. The distribution was followed by the elution of radiolabeled $^{14}CO_2$ (Liquid Scintillation Counting technique).

2. The study design was similar to the US EPA Fate & Transport guidelines Series 835.

3. The GLP as required by EPA were not followed; however, the registrants claim that the GLP of the OECD guidelines were followed.

4. Concentrations of the test substance were 110, 384 and 990 µg/L and the removal respectively was 99.9%, 99.8% and 99.9%. Of which 69% was through biodegradation.

5. The duration of the study was 54 days for one test unit 1 and 63 days for the test unit 2.

6. Instrument specifications and running conditions were not provided.

7. The limit of detection for LSC was not reported.

8. No information was provided for the preparation of CAS test solutions.

9. Study attachments 5B, 8B and 9B , labeled "reproduced from the best available copy" were illegible.

10. The lab which conducted the study was not identified.

RASSB's Conclusions & Recommendations:

RASSB concludes that the study is unacceptable in the present format and if the registrants provide the following additional data, the Agency will give due consideration for acceptance of the submission:

a. Limit of detection (LOD) for LSC

b. Identification and location of the analytical laboratory where the study was conducted.

c. Provide a copy of OECD's Good Laboratory Practices (GLP).

d. Provide legible copies of study attachments 5B, 8B and 9B.

e. Provide the procedure for the preparation of CAS test solution

SUMMARY OF RASSB CONCLUSIONS:

Study	MRID#	Recommendation
A	444349-14	Reject
B	444349-15	Upgradable
C	444752-05	Reject
D	444752-06	Upgradable

The Agency has noted that environmental fate data collected and submitted in the studies A, B, C and D were on dodecyl dimethylamine oxide and not on the active compound (alkyl (C_{10-16}) dimethylamine oxide) for Cleaning Magic I.

In general, all submissions suffered from the flaw that the protocols for the studies were mentioned but were never submitted with a study, specification and running conditions of the analytical techniques were also not submitted , temperature and pH of the samples were either not maintained or not mentioned. QA/QC's procedures were invariably missing.

RASSB recommends that P & G provide the additional data for studies B & D as noted above.

RASSB also recommends that P & G Company should resubmit the studies (A & C) conducted according to the OPPTS Test Guidelines Series 835 for the Fate, Transport and Transformation, which the Agency can accept as a supplemental information.

RASSB concludes that a hydrolysis study is required, since this study will likely provide relevant information about the stability of the parent substance and/or its transformation product that can be used to assess the surface and ground water contamination and may also be used for determining dietary exposure.

cc: Chemfile: 00439 (Nshamim)

Attachments: Versar's reviews.