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THE PROCTER & GAMBLE COMPANY

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SHARON WOODS TECHNICAL CENTER



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September 12, 1984

CINCINNATI, OHIO 45241

Dr. Arthur Stern
Acting Executive Secretary
TSCA Interagency Testing Committee
Environmental Protection Agency [TS-796]
401 M Street, S.W.
Washington, D.C. 20460

Contains No. 9
RECEIVED
OCT 10 1984
AM 9:17

RE: CHEMICALS TO BE REVIEWED BY THE TOXIC SUBSTANCES
CONTROL ACT INTERAGENCY TESTING COMMITTEE
(48 FEDERAL REGISTER 51519 11/9/83)

Dear Dr. Stern:

This presents the comments of the Procter & Gamble Company and its subsidiaries on the notices identified above. These comments are filed in our individual behalf by Procter & Gamble as a processor of one of the materials listed.

In the Federal Register (48 FR 51519), the Interagency Testing Committee published a list of chemical substances which are under review for possible recommendation to the EPA Administrator for testing for adverse health and environmental effects pursuant to Section 4 of TSCA. This notice also advised that the ITC would accept comments on the listed chemicals. In response to this request, we would like to submit the attached information on one of the substances identified in that listing: D1 (C₁₄-C₁₈) alkylmethylamines (CAS Registry Number 67700-99-6). Procter & Gamble is a processor of this material which is also referred to as ditallow methylamine (DTMA).

The attached information establishes that DTMA has been extensively evaluated for both human effects (acute and subchronic) and environmental effects. These studies show that the levels of DTMA which could affect human health or the environment are well above the levels expected to be present in the environment or to be encountered by humans. Thus, we conclude that not only has DTMA been well studied, but that those studies indicate that it is not likely to pose an unreasonable risk to either human health or the environment. We therefore recommend that the ITC remove this material from further consideration for regulation under Section 4 of TSCA.

We appreciate this opportunity to assist the ITC in its review of selected chemical substances. We hope the information provided is of value to the committee.

Sincerely,

THE PROCTER & GAMBLE COMPANY

T. W. Mooney
Manager, Technical Government Relations

DI (C₁₄-C₁₈) ALKYL METHYLAMINES
CAS Reg. Nos. 67700-99-6 and 68603-65-6

This document summarizes the results of unpublished safety studies on commercially produced di (C₁₄-C₁₈) alkylmethylamines, also referred to as ditallow methylamine (DTMA). Testing reported here was sponsored by the Procter and Gamble Company and conducted either in-house or by qualified independent testing facilities.

BACKGROUND

Commercial DTMA is a white solid (paste) which is essentially 100% active (tertiary amine) containing small and varied amounts (<5%) of primary and secondary amine. Unless otherwise stated, results reported in this summary are expressed on the basis of total amine as measured in the tested samples.

Ditallow methylamines (fatty amines) and their derivatives are used in a wide range of commercial applications, primarily as chemical intermediates. The Procter & Gamble Company uses DTMA, along with cationic surfactants, in the formulation of fabric softeners. DTMA adheres to fabric imparting a soft surface feel and reduces the formation of static electrical charges ("static cling").

USAGE

Industry wide usage of DTMA in fabric softeners is estimated at 5×10^6 lbs/yr. Other industrial uses of DTMA and its derivatives include anti-static agents, corrosion control agents, foam stabilizers and emulsifiers.

OVERALL SUMMARY

Extensive testing of DTMA has been conducted to assess its acute and subchronic toxicity as well as its genotoxic and teratogenic potential. Results of these studies together with data on occupational and consumer exposure levels indicate no hazard to human health is associated with use of DTMA in fabric softeners.

The environmental safety of commercial DTMA, as it is used and disposed of via its production and use in consumer products, has been established. Laboratory tests show that DTMA: 1) is completely biodegraded at a moderate rate, 2) is effectively removed from sewage by conventional treatment methods, 3) has aquatic safety factors greater than 10,000 based on acute fish and invertebrate toxicity relative to estimated surface water concentrations, and 4) exhibits low potential for bioaccumulation.

The long term use of DTMA in fabric softeners provides extensive experience with consumer exposure and the related disposal of DTMA to sewage treatment systems. To our knowledge, this use has not resulted in any adverse effects on human health or the environment.

In summary, all information on DTMA demonstrates its use in fabric softener products is safe from the viewpoint of human health and presents no environmental hazards. Details follow.

I.

**HUMAN SAFETY ASSESSMENT
OF COMMERCIAL DI (C₁₄-C₁₈) ALKYL METHYLAMINES (DTMA)**

A. Acute Toxicity

All animal and human testing described below was conducted using essentially 100% active (total amine content) DTMA.

1. Oral - A 75% w/v mixture of DTMA in mineral oil was administered to rats by gavage at 20 ml/kg. Animals were observed for a 14-day post-exposure period for mortality. The minimum lethal dose (LD₁) was greater than 15 gm/kg, the highest dose tested.

Intragastric administration studies of 10 ml/kg and 20 ml/kg of 75% w/v DTMA in mineral oil in dogs found mild to negligible emesis and catharsis along with mild transient gastric effects (hyperemia, petechiae, and darkened mucosa). Mineral oil alone is a mild laxative.

2. Percutaneous - Undiluted DTMA was applied occluded to clipped backs of rabbits at a dose level of 2 gm/kg for 24 hours. Animals were observed for a 14-day post-application period for mortality. The minimum lethal dose (LD₁) was greater than 2 gm/kg, the highest dose tested.
3. Ocular - Rabbit eye testing of an undiluted product containing about 20% DTMA and 20% ditallow dimethyl ammonium chloride produced essentially no irritation, when 0.01 ml was instilled on the cornea.

4. Skin Irritation -

Animal Test - 50% w/v aqueous and 5% w/v aqueous dispersions of DTMA were applied occluded to the clipped intact and abraded backs of rabbits at a dose of 0.4 ml/patch for 24 hours. The test sites were graded 30 minutes and 48 hours after patch removal; mild skin irritation was observed.

Human Test - Skin irritation tests (a single 24-hour, and three 24-hour exposures over a 6-day period) with aqueous dispersions of DTMA (0.3 ml/occluded patch) showed little or no skin irritation at the concentrations tested, 1.0 and 2% w/v aqueous.

The concentration of 2.0% w/v aqueous DTMA gave 9 mg DTMA/in² of patch. This is 300-fold above the level of DTMA on fabric (0.03 mg DTMA/in²) to which consumers would be exposed during the wearing of softened clothing.

5. Skin Sensitization -

Animal Test - 30% w/v DTMA in 80%/20% ethanol/water was applied (0.4 ml per each occluded patch) to the clipped backs of 20 guinea pigs for six hours, once a week, during a three-week induction period. Challenge with 20% w/v DTMA in 80%/20% ethanol/water for a single 6-hour occluded exposure occurred two weeks after completion of induction. No evidence of skin sensitization was observed.

Human Test - 192 volunteer subjects received nine exposures to 2% w/v aqueous DTMA (0.3 ml/occluded patch) applied for a 24-hour period, three times a week during a 3-week induction period. Challenge with 2% w/v DTMA as a single 24-hour occluded patch occurred two weeks after completion of the induction period. No evidence of skin sensitization was observed.

B. Subchronic Toxicity

1. Oral - Rats were fed 0.6, 6 and 30 mg/kg/day DTMA in their diet for 13 weeks. A control group received untreated diet. All groups contained 20 males and 20 females.

No treatment-related changes in clinical condition were found. There were no treatment-related changes in body weights, food consumption, or hematology values. Pathology findings consisted of accumulations of histiocytes in the mesenteric lymph nodes of 6 and 30 mg/kg/day rats. The severity of the histiocytosis was dose-related and the mesenteric lymph nodes of most 30 mg/kg/day rats were enlarged at necropsy. No histiocytosis was found in 0.6 mg/kg/day rats.

From these results, the oral no-observable-effect level (NOEL) was 0.6 mg/kg/day. This is at least 100,000-fold above the anticipated oral daily human exposure to DTMA via drinking water.

2. Percutaneous - Rabbits were treated topically with 2 ml/kg/day of DTMA at dose levels of 5 or 50 mg/kg/day, five days per week for 13 weeks. A control group received the vehicle, polyethylene glycol 600. All groups contained five males and five females.

No treatment-related clinical changes were observed. A slight decrease in body weight gain was recorded for 50 mg/kg/day animals during the last seven weeks.

Moderate irritation (erythema, edema, desquamation, fissuring and atonia with wrinkling) was produced in 50 mg/kg/day animals. A mild dermal response was seen in most 5 mg/kg/day animals.

There were no treatment related changes in organ weights or hematology values. Pathology findings were consistent with a moderate degree of irritation at the application site in 50 mg/kg/day rabbits. A minimal epidermal response was seen in 5 mg/kg/day animals. Examination of other tissues revealed intralobular leukocyte foci in the liver and epithelioid cells in the mesenteric lymph nodes of several 50 mg/kg/day rabbits. These lesions have no known toxicological significance. No liver or lymph node changes were found in 5 mg/kg/day animals.

From these results, the no-observable-effect level (NOEL) was 5 mg/kg/day. This is at least 70-fold above the anticipated daily skin exposures to DTMA from softened clothing.

C. Genotoxicity

DTMA was found to be non-mutagenic in Ames, mouse lymphoma, rat in vivo cytogenetics, and rat hepatocyte unscheduled DNA synthesis testing.

1. Ames Test - No evidence of mutagenicity was observed in testing DTMA in tetrahydrofuran in the Ames test. Five tester strains of Salmonella (TA98, TA100, TA1535, TA1537, and TA1538) were used, both with and without metabolic activation by Aroclor-induced rat liver microsomes.
2. Mouse Lymphoma Assay - DTMA in tetrahydrofuran was negative in the L5178Y TK +/- mouse lymphoma assay. This testing was run both with and without metabolic activation by Aroclor-induced rat liver S-9 fraction.
3. Rat In Vivo Cytogenetics - DTMA in corn oil dosed by gavage for 5 days did not induce a significant number of chromosomal aberrations.
4. Unscheduled DNA Synthesis - DTMA in ethanol did not induce unscheduled DNA synthesis in primary cultures of rat hepatocytes.

D. Teratogenicity

Rabbits were treated with DTMA by gavage at dose levels of 50, 250, or 1000 mg/kg daily from day six to day 18 of gestation (the period of organogenesis) inclusive. A control group received the vehicle, corn oil. All groups contained 16 females. Reproductive performance, clinical conditions, gross necropsy changes and the outcome of gestation were assessed. Administration of 250 mg/kg/day DTMA produced slight maternal toxicity but no embryoletality, direct embryonic growth retardation or teratogenic effects.

No direct retardation of embryonic growth or teratogenic effects were noted at 1000 mg/kg/day DTMA. However, due to a possible association of treatment at 1000 mg/kg/day with embryoletality, 250 mg/kg/day DTMA was considered the highest no-observable effect level (NOEL). This is several thousand-fold above the anticipated daily skin exposure of consumers to DTMA from softened clothing, and about forty million times the maximum human exposure through drinking water.

E. Human Exposures to DTMA

Assessments of both occupational and consumer (i.e., 70 kg adult and 9.5 kg child) exposures are summarized below.

1. Occupational Exposures

Exposure to DTMA via inhalation and/or percutaneous absorption as employees handle raw materials is negligible since DTMA is stored in sealed tanks until manufacturing of the finished product. When appropriate, safety glasses and impervious clothing are worn. Exposure to DTMA via percutaneous absorption during the manufacturing and packing of finished fabric softener is negligible and usually occurs only during quality control sample taking. Exposure via the inhalation route is negligible due to existing workplace practices and the very low vapor pressures of DTMA.

2. Consumer Exposure

a. Skin Exposures

The main exposure to DTMA in fabric softeners is from skin contact during the wearing of treated fabrics. Limited (acute) skin contact also occurs from handling the DTMA-containing product.

Assuming the fingertip area of both hands touches the DTMA-containing softener product, an adult could have a brief exposure to DTMA of 0.2 mg/kg. Based on measured levels on clothing, and transfer from clothing to skin, for a similar compound, subchronic consumer dermal exposures to DTMA are estimated to be 0.04 mg/kg/day for adults, and 0.07 mg/kg/day for children.

These dermal exposures are well below safe acute and subchronic dermal exposure levels established from animal studies (i.e., at least 1,500-fold below the acute dermal minimum lethal dose and at least 70-fold below the subchronic dermal no-observable-effect level).

b. Oral Exposures

Oral exposures to DTMA-containing products can result from the accidental ingestion of finished product. Also, there is a slight potential for exposure of the general population to very low levels of DTMA via drinking water (see Section II, E.4).

Rat acute toxicity studies for DTMA containing fabric softeners show that the minimum lethal dose (LD₅₀) was greater than 20 gm/kg, or practically nontoxic. Further assurance of the safety of DTMA containing fabric softeners comes from the careful monitoring of human health-related comments; no oral toxicity safety concerns have been identified.

From Section II.E.4., the maximum drinking water concentration of DTMA is 0.0002 mg/l. This gives a potential adult or child exposure to DTMA from drinking water of 0.000006 mg/kg/day based on a drinking water consumption of 2 l/day⁽⁷⁾ or 0.3 l/day⁽⁸⁾ for an adult or child, respectively. Exposure to DTMA in drinking water is 100,000-fold below the subchronic oral no-observable effect level.

c. Conclusion

Virtually all of the projected daily consumer exposure to DTMA from fabric softeners is from the wearing of softened clothing. All estimated long-term consumer exposures are well below the no-observable-effect-levels found in subchronic animal studies.

Finally, careful monitoring and follow-up of consumer and occupational comments allow for further assurance of the safe use of DTMA in fabric softeners; no adverse impact on human health has been found. Thus, DTMA as used in fabric softeners is safe from the viewpoint of human safety.

II.

ENVIRONMENTAL SAFETY ASSESSMENT
OF COMMERCIAL DI (C₁₄₋₁₈) ALKYL METHYLAMINES (DTMA)

A. Treatability

Based on laboratory scale testing, DTMA is effectively removed by typical sewage treatment systems and is not expected to affect wastewater treatment processes at a predicted influent sewage concentration of 0.056 mg/l. (See Sec. E)

1. Results of semi-continuous activated sludge treatability tests indicate that DTMA undergoes greater than 90% removal when fed at 20 ppm. Removal was measured by both loss of chemical reactivity with disulfine blue (93%) and removal of soluble organic carbon (>90% within 24 hours).
2. No toxicity to activated sludge organisms was seen at 200 mg/l (highest level tested) in a microbial inhibition test. This test method measures the metabolism of ¹⁴C-glucose after a 2 hour exposure to DTMA. These data indicate that there is a high degree of safety relative to predicted sewage concentrations.

B. Biodegradability

In laboratory biodegradation studies, DTMA was shown to undergo complete ultimate biodegradation at a moderate rate. At 10 and 20 mg/l, up to 82% of theoretical CO₂ was evolved from dilute bio-reactors (1% activated sludge seed) over a period of 55 days. Degradation rates appear to be solubility limited.

C. Aquatic Toxicity

Laboratory tests indicate that DTMA has a moderate level of acute toxicity to aquatic organisms. These toxicity data, in conjunction with the low (0.0016 mg/l) expected exposure levels to DTMA in surface water (see next section), afford high safety factors for aquatic organisms.

1. Acute (96-hour LC₅₀) toxicity of DTMA to bluegill are 23 mg/l and 180 mg/l in laboratory reconstituted water and surface water, respectively. The calculated acute safety factor in surface water is 112,500.
2. Acute (48-hour LC₅₀) toxicity to the invertebrate Daphnia magna shows a similar pattern ranging from 3.1 mg/l in laboratory reconstituted water to 21 mg/l in surface water. The calculated acute safety factor for Daphnia in surface water is 13,125.

The higher LC₅₀'s in surface water relative to laboratory reconstituted water can be explained on the basis of chemical and physical reactions of DTMA with materials naturally present in surface water (suspended solids, and organic anions) which reduce DTMA bioavailability through sorption and complexation.

3. Laboratory tests with algae in Algae Assay Procedure (AAP) medium indicate that these organisms may be particularly sensitive to DTMA. Chronic tests with *Selenastrum* show algal static effects at 0.052 µg/l. Similar testing with equimolar levels of an anionic surfactant (Linear Alkylbenzene Sulfonate) present show a 10 fold reduction in observed toxicity to 0.57 mg/l. The algal static concentrations for *Microcystis* and *Navicula* in AAP medium were 0.96 mg/l and 4.6 mg/l respectively. Amplification of toxicity to algae by surface water components is expected, as seen in the acute studies with other organisms. Since anionic surfactant levels can be expected to be well in excess of those for DTMA, the resulting minimum calculated chronic safety factor for DTMA in surface waters is >356 (0.57 ÷ 0.0016).

D. Physical/Chemical Properties

DTMA demonstrates very low water solubility which probably accounts for its moderate rate of biodegradability. No significant bioconcentration is expected, however, based on the measured octanol/water partition coefficient.

1. Solubility in deionized water was measured after 14 days using an HPLC/conductivity detector. Results show an apparent solubility of 0.29 mg DTMA/l.
2. The octanol/water partition coefficient, measured at two concentrations after 8 and 24 hours, was log p = 3.15. Based on published correlations⁽¹⁾, these data would predict a bioconcentration factor of 146.

E. Expected Environmental Concentrations of DTMA

Industry wide usage of DTMA in wash-day fabric softeners used by consumers is estimated to be (5x10⁶ lbs/yr)⁽²⁾. The principal route of environmental entry of this DTMA will be via wastewater treatment systems. As the previous laboratory data indicate, DTMA environmental concentrations will be significantly reduced in these systems by biodegradation and adsorption.

1. Raw Wastewater Concentration

In 1980 the U.S. population was approximately 220x10⁶⁽³⁾ and the average per capita wastewater flow was 134 gallons/capita/day⁽⁴⁾. Thus, the average concentration of DTMA in wastewater is calculated to be:

$$\frac{5 \times 10^6 \text{ lb/yr}}{220 \times 10^6 \text{ capita} \times 134 \text{ gal/capita/day}} \times \frac{454,000 \text{ mg/lb}}{365 \text{ day/yr} \times 3.79 \text{ l/gal}}$$

= 0.056 mg DTMA/l of raw wastewater

2. Sewage Effluent Concentration

Results of model activated sludge testing show that at least 90% of DTMA is removed (via a combination of adsorption and biodegradation) by these wastewater treatment systems. Currently, approximately, 80%⁽⁵⁾ of sewage undergoes secondary treatment. Assuming, conservatively, that no DTMA is removed from the remaining 20% of sewage, the following calculation predicts the national average level of DTMA in sewage effluent:

(0.8 treated) (10% DTMA not removed) (0.056 mg/1 DTMA)
+ (0.2 untreated) (100% DTMA not removed) (0.056 mg/1 DTMA)
= 0.016 mg of DTMA/1 of Sewage Effluent

3. Surface Water Concentration

Sewage effluent is commonly discharged into rivers and streams. The dilution factors for 161 major river basins were calculated and the average dilution factor was determined to be 100⁽⁶⁾. In fact, 91% of river basins examined had dilution factors greater than 10⁽⁶⁾. However, to be conservative, the factor of 10 is used to estimate the maximum concentration of DTMA in surface water as follows (does not take into account anticipated removal in surface water via biodegradation and adsorption):

0.0157 mg DTMA/1 x 0.1 dilution
= 0.0016 mg DTMA/1 of surface water

4. Drinking Water Concentration

The level of DTMA estimated for drinking water will be considerably lower than that estimated for surface water and well below analytical detection. Each of the following factors will contribute to the reduction:

- a. the potential for DTMA to adsorb to solids will result in removal of DTMA from surface water.
- b. continued biodegradation in surface waters and sediments will further reduce DTMA levels.
- c. removal of any remaining DTMA by drinking water treatment (flocculation and sedimentation) is expected to be significant.

Also, since the average dilution factor for effluent wastewater in major U.S. rivers is 100⁽⁶⁾ and surface waters used as drinking water sources are typically those surface waters which are not severely impacted, a dilution factor of 100 is used to estimate drinking water concentration from wastewater effluent concentration. Using just this dilution factor and ignoring the potential reduction in DTMA levels by the above factors results in the following maximum drinking water concentration:

0.0157 mg DTMA/1 x 0.01 dilution
= < 0.0002 mg DTMA/1 of drinking water

REFERENCES

1. Veith, G. D. et al in Aquatic Toxicology, J. G. Eaton, et al ED. (1980).
2. Estimate based on potential industry wide usage in fabric softeners.
3. U.S. Bureau of Census 1979 "Statistical Abstract of the U.S." Washington, D.C.
4. U.S. EPA, "Municipal Waste Facilities Inventory" Division of Technical Support, Washington, D.C. (1976).
5. Chamblee, J. A. Municipal Pollution Abatement Report Card. JWPCF 54 Vol. 5 p. 422. (1982).
6. Holman, W.F., "Estimating the Environmental Concentrations of Consumer Product Components". Presented to the 4th ASTM Symposium on Aquatic Toxicity, October 16-17, 1979.
7. Connor, M. S., "Comparison of the Carcinogenic Risks from Fish vs. Groundwater Contamination by Organic Compounds". Environ. Sci. Technol. 18, pp. 628-631 (1984). Note: The EPA's Carcinogen Assessment Group uses an average daily consumption of two liters of drinking water for a 70-kg man.
8. Rupp, B. M., "Age Dependent Values of Dietary Intake for Assessing Human Exposure to Environmental Pollutants". Health Physics 39, pp. 151-163 (1980). Note: The range of daily drinking water consumption for a one year old child was 0.16 to 0.34 liter. This includes tap water intake as well as water used for mixing formulas and fruit juices.
9. Buehler, E. V., "Delayed Contact Hypersensitivity in the Guinea Pig", Arch. Dermatology 91, pp. 171-177 (1965).
10. Feldmann, R. J. and Maibach, H. I., "Penetration of ¹⁴C Hydrocortisone Through Normal Skin. The Effect of Stripping and Occlusion". Arch. Dermatology 91, pp. 651-666 (1965).