WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTE

FOOD AND AGRICULTURE ORGANIZATION
ORGANISATION POUR L'ALIMENTATION ET L'AGRICULTURE

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DATA SHEET ON PESTICIDES

No. 80

DEET

CLASSIFICATION:

Primary Use: Insect repellent

Secondary Use: None

Chemical Group: **Substituted toluamide**

1.0 GENERAL INFORMATION

1.1 COMMON NAME: Deet (ANSI, ESA, exception BPC, BSI, E-ISO, diethyltoluamide)

1.1.1 Identity:

IUPAC: N, N-diethyl-m-toluamide

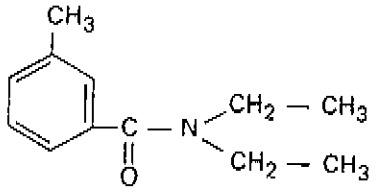
CAS: N, N-diethyl-3-methylbenzamide

CAS Reg. No.: 134-62-3

Molecular formula: $C_{12}H_{17}NO$

Molecular weight: 191.3

Structural formula:



1.1.2 Synonyms: Autan^{R}; DET; DETA; Detamide^{R}; Dieltamid^{R}; diethyltoluamide; diethyl-m-toluamide; ENT 20,218; ENT 22542: Flypel^{R}; m-Delphene^{R}; m-Det; m-Deta; Metadelphene^{R}; MGK; Naugatuck DET^{R}; OFF^{R}; Repper-DET; Repudin Special^{R}.

1.2 SYNOPSIS: Deet is a selected spectrum, non-cumulative substituted toluamide; an insect repellent of slight toxicity to mammals and with residual activity. The technical product is listed in WHO Hazard Class III. Toxicity is not increased after metabolism to the oxygen analogue. Deet was introduced commercially in 1955.

1.3 SELECTED PROPERTIES

1.3.1 Physical characteristics - The technical product is a nearly odourless, colourless to amber liquid consisting of 85-95% meta-isomer. The boiling point is 111°C at 1.0 mm Hg; the density (d) $^{24}_{4}$ is 0.996 to 0.998; viscosity 13.3 mPa at 30°C; the refraction index (n) $^{25}_{D}$ 1.5206. Deet is not corrosive to metals.

1.3.2 Solubility - Practically insoluble in water and glycerin. Miscible with ethanol, isopropanol, propylene glycol, and other organic solvents.

1.3.3 Stability - Technical deet is relatively stable, highly hygroscopic and light sensitive. Sensitive to strong acids and alkalis.

1.3.4 Vapour pressure - 2.54×10^{-3} mm Hg (25°C)

1.4 AGRICULTURE, HORTICULTURE AND FORESTRY - No recommended uses.

1.5 PUBLIC HEALTH PROGRAMMES - See 1.6

1.6 HOUSEHOLD USE

1.6.1 Common formulations - Deet is commercially available as emulsifiable concentrate, creams, sticks, lotions and in pressurized sprays and foams, ranging in concentration from 11.27 to 99.9% deet. It may be formulated with solvents such as ethanol or isopropanol, or with other pesticides.

1.6.2 Susceptible pests - Blood-sucking insects (including mosquitoes, blackflies, gnats and other biting fleas), mites and ticks.

1.6.3 Use pattern - World-wide, on human skin to repel insect pests. Can be used on clothing, household pets, tents, bedrolls and screens.

1.6.4 Unintended effects - No information available.

2.0 TOXICOLOGY AND RISKS

2.1 TOXICOLOGY - MAMMALS

2.1.1 Absorption routes - Deet is absorbed slowly through the skin, gastrointestinal tract or by inhalation of spray mist. Maximum dermal penetration occurs within 24 hours and depending upon the vehicle and the species may account for up to 77% of the applied dose, the remainder being evaporated.

2.1.2 Mode of action - The exact mode of action of deet is not known. Circumstantial evidence implicates deet in activities causing accumulation of potassium in muscle cells and neurons. See Section 2.1.7. Pharmacological effects.

2.1.3 Excretion products - In seven-day excretion studies in rats, rabbits and dogs, topically applied radio-labelled deet (75% m-Deet in ethanol) was found to be excreted primarily through the urine with the dog having lowest absorption potential. Of absorbed deet >75% was excreted in the urine within 24 hours with little accumulation in any tissues for the three species. Published human studies indicated that most of absorbed deet is excreted unchanged within one hour with the remainder being metabolized. The

predominant metabolic pathway in man involves oxidation of the benzylic moiety and hydroxylation of the side chain yielding m-carboxyl-N,N-diethybenzoylamide. The mono-hydroxylation product is excreted as a glucuronide conjugate rather than a free alcohol.

2.1.4 Toxicity - Single dose

Technical grade

Oral LD_{50}:

Rat (M)	2.00 g/kg b.w. (meta-isomer)
	1.21 g/kg b.w. (ortho-isomer)
	2.30 g/kg b.w. (para-isomer)

Administration of technical grade deet to male rats by gastric intubation led to acute toxicity symptoms including hyperemia at base of ears, lacrimation, depression, prostration, epileptoid tremors, asphyxial convulsions, respiratory and cardiac failure and death. Doses near but below the LD_{50} caused slight to mild symptoms. Some rats appeared moribund but recovered completely within 24 hours. No latent toxic effects were observed.

Dermal LD_{50}:

Mouse (M,F)	4.5 g/kg b.w.
Rat (M,F)	>5.0 g/kg b.w.
Rabbit (M)	3.18 g/kg b.w.

Inhalation LC_{50}:

Rat (M,F)	>5950 mg/m^3/8h

Rats exposed to concentrations of 3.15 mg/l/hr for two to six hours experienced a slight bloody discharge from the nose. After 24 hours the rats appeared normal and showed no significant physical or histopathological changes.

Intravenous LD_{50}:

Rabbit (M,F)	>50 mg/kg b.w. (meta-isomer)

All rabbits receiving >75 mg/kg b.w. in a single injection died within one minute. Rabbits receiving 50 mg/kg b.w. experienced temporary miosis and respiratory stimulation. Pregnant rabbits injected intravenously with a radio-labelled m-deet in ethanol solution on the fifteenth day of gestation did not bioaccumulate deet; the foetuses contained approximately one-sixth of the maternal blood level of deet at all sampling intervals.

Eye irritation - Exposure of the rabbit eye to three drops (0.04 mg m-deet/drop) of a 30% and 40% solution of deet in cottonseed oil and undiluted deet resulted in edema of the nictitating membrane, lacrimation, conjunctivitis with pus. After 48 hours mild to moderate conjunctivitis and cloudiness of the cornea were present. After five days, injury to the eye began to disappear, leaving no permanent damage..

2.1.5 Toxicity, repeated doses

Oral - Male rats, given 10% ortho-isomer (600 mg/kg b.w.) or 12.5% para-isomer (1125 mg/kg b.w.) for 19 days by gavage showed no evidence of adverse effects and no histopathological changes.

Male rabbits, given 528 mg/kg b.w. m-deet daily by gavage for 15 days showed progressive weight loss, decreased serum calcium levels, increased cholesterol and triglyceride levels as well as increased relative kidney weight.

Dermal - Female rabbits dosed with radio labelled m-deet in ethanol (75% conc.) throughout gestation in doses ranging from 0 to 500 mg/kg/b.w./day absorbed about 45% of the applied dose. The degree of absorption was not dose dependant. No radioactivity was observed in the full term foetuses.

Moderate erythema, desquamation and dryness of skin occurred when rabbits were dosed with m-deet in cottonseed oil or isopropanol (50% conc.) at 1.0 g/kg b.w./day for 65 days. Later, the skin application site became leathery with hard, dry fissures developing. Three weeks after the final application all rabbits appeared normal except for occasional scarring and no evidence of skin sensitization was found.

In a 60 day study horses sprayed with 31 g/day of m-deet in aerosol formulations (3.75-75.0% conc.) developed hypersteatosis and dermatosis at >15% conc. The timing of appearance of these effects was inversely related to dose.

Studies done on ortho- and para-isomers of deet showed similar results to the meta-isomer. Dermal application of 200 mg/kg b.w./day to rabbits for 65 days resulted in mild interstitial nephritis and more extensive inflammatory kidney lesions with the para-isomer.

Inhalation - Groups of rats exposed to air saturated with m-deet. 100 mg/1.4m^3 for 40 hours (eight hours/day, five days per week and for seven weeks) showed slight hyperemia of ears, feed and tail and increased motor activity. Some rats showed slight bleeding from the nose. At the end of the study there were no significant physiological or histopathological findings.

2.1.6 Dietary studies

Short-term - In a 200-day rat feeding study with dose levels of 100-10000 mg/kg diet, no effect levels were established at 500 mg/kg/diet for males and 5000 mg/kg/diet for females. The male no effect level was due to induced hypertrophy of the testes. Hypertrophy of the liver and kidneys was observed in both sexes. No histopathological changes were reported.

2.1.7 Supplementary studies

Carcinogenicity - Lifetime studies of female mice and male and female rabbits dosed twice a week with deet in acetone (100, 50 and 10% conc.) at a volume of 0.02 ml showed no carcinogenic activity in either species and no local changes in mice.

Mutagenicity - Deet had no mutagenic potential in the metabolically activated and non-activated Ames Salmonella/mammalian microsome mutagenicity assay, nor in tests involving Escherischia coli.

Additionally, a dominant lethal assay in male mice using m-deet in corn oil yielded no statistically significant results.

Teratogenicity - No evidence of teratogenic activity was found when female rabbits were repeatedly dosed dermally throughout gestation a 75% solution of m-deet in concentrations ranging from 50 to 1000 mg/kg b.w./day. In a rat combined reproduction and teratogenicity study, dermal applications of 100 or 1000 mg/kg b.w./day of m-deet for the duration of gestation caused no observed teratologic effects.

Reproduction

Parent effects - Male rats inhaling 1500 mg m-deet/m^3 of air for six hours/day, five days/week for 13 weeks had sperm head abnormalities and reduced sperm motility. Untreated females mated with these males had a decreased pregnancy rate.

In female rats dermally dosed with m-deet at 100 and 1000 mg/kg b.w./day for the duration of pregnancy, increased pre- and post-implantation losses and decreased foetal viability and foetal weight were observed at the highest dose level. At 100 mg/kg/day, only the viability of foetuses was adversely affected. These adverse effects were confirmed in a second study, using similar doses for a period of one to six months prior to mating. In addition, adverse testicular effects and decreased sperm motility were reported in treated males at both dose levels. In another different study, groups of male rats dermally dosed with m-deet at doses up to 1000 mg/kg b.w./day, five days/week for nine weeks showed no alteration in sperm count, sperm morphology, sperm viability, body weight or food consumption at any dose level.

Pup Effects - When female rats were dosed dermally with m-deet retarded development of the newborns was observed at the 1000 mg/kg, the highest dose level tested.

Neurotoxicity - When the mice were injected once, intraperitoneally with 40% m-deet in alcohol they showed motor excitement, disturbed coordination, convulsive twitching of limbs, depression and death. Dogs administered 100-300 mg/kg b.w./day of m-deet for 13 weeks experienced mild CNS stimulation and occasional emesis. Temporary miosis was reported in rabbits following a single intravenous injection of 50 mg/kg b.w.

Sensitization and skin irritation - Deet was not found to cause a photo-chemical irritation reaction when applied dermally to rabbits prior to UV light exposure. No evidence of sensitization was observed in guinea pigs following dermal application of 1.0 ml of 10% m-deet solution.

Behavioural changes - Minor behavioural changes in passive and quick avoidance, tactile sensitivity, endurance, balance and level of activity, were seen in a 65 day rat inhalation study of m-deet at all dose levels from 250-1500 mg/m^3.

Pharmacological effects - A 40% emulsion of m-deet (in vegetable lecithin, ethanol and distilled water) had no effect on isolated rat uterus at a dilution of 1:10000. A dilution of 1:5000 depressed the amplitude of rhythmic contraction in the uterus while a dilution of 1:2500 completely abolished contraction and muscle tone. All effects were reversible when the m-deet emulsion was removed or upon additional treatment with acetylcholine or barium chloride. The effects, therefore, are consistent with increased intracellular potassium levels. Rabbits showed circulatory and respiratory responses to m-deet including a slight but evanescent fall in blood pressure when intravenously administered at 5 mg/kg b.w.

2.2 TOXICOLOGY - MAN

2.2.1 Absorption route - See 2.1.1

2.2.2 Dangerous doses - No published information available. Probable oral lethal dose 0.5 to 5.0 g/kg b.w. Dermal lowest toxic dose 35 mg/kg b.w./five days.

2.2.3 Observations of occupationally exposed workers - Contact dermatitis developed on facial skin of 2.3% of workers using m-deet lotion. Hyperemia and pronounced edema of fingers, dryness and superficial cracks, tenderness in region of the fingers and periodic numbness followed by the sensation of pain in the fingers were common observations.

2.2.4 Observations of volunteers - In 1966, three preparations of deet were tested in 85 men aged 19 to 27 years for adverse dermal effects. Deet (40%) in alcohol was applied to hands, forearms, face and neck at a daily dose of 4 to 6 ml for three to four weeks. Effects included seborrhea (three cases), contact dermatitis (one case), acne-like eruptions (one case), and conjunctivitis (one case).

A group of 232 human volunteers' clothing was sprayed once every three to five days for one to one and one half months with a deet formulation including deet and Neopynamin or Sumithrin. No side effects were seen on the skin.

Five human volunteers were tested with a 50% solution of deet. One ml was applied to the face and 2 ml were applied to each arm daily for five days. Tingling and mild desquamation occurred around the nose. No systemic effects were observed. Desquamation cleared after two days.

2.2.5 Observations of the general population - No published information available. Bystander exposure is not likely to occur when recommended application procedures are used. However, extra care should be taken to avoid unintentional exposure of young children and other sensitive individuals through mouth or skin contact with liberally treated persons or objects (e.g. clothing, bedding, toys, etc.).

2.2.6 Reported mishaps - The majority of adult mishaps reported between 1961-1981 produced only mild symptoms of irritation. Most individuals remained asymptomatic. Contact urticaria has been reported in several cases in the general population.

Ten soldiers experienced bullous eruptions in the antecubital fossae, 18 to 24 hours after application, prior to sleep, of a 50% m-deet repellent formulation to their skin. Observations included burning sensation, erythema, blisters, ulceration and scarring.

Mishaps in which deet may have been concerned, produced severe toxic encephalopathy occurred in female children; two of nine poisonings were fatal. An 18 month old girl was hospitalized following ingestion of a small amount of 10% deet formulation. Recovery was slow, after six weeks of treatment the patient was discharged to a second hospital for further convalescence. No further details about her recovery are available.

A five year old girl, sprayed nightly for three months with a formulation (10% deet) died 24 days after admission to hospital for symptoms of toxic encephalopathy. At autopsy, edema of the brain and congestion of the meninges were observed.

A three and one half year old girl was admitted to hospital with symptoms of toxic encephalopathy after cumulative exposure to approximately 180 mg of deet (15%) over a two week period. Improvement followed vigorous medical treatment, including anti-convulsant therapy. The patient was discharged after three days in hospital.

A six year old girl died seven days after admission to hospital presenting toxic encephalopathy following repeated exposures to a 15% deet formulation. This patient was also a presumed heterozygote for ornithine carbamoyl transferase deficiency.

2.3 TOXICITY TO NON-MAMMALIAN SPECIES

2.3.1 Fish - LC_{50} (24 and 48 hr. exposure)

Gambusia affinis (Mosquito fish) 235 mg/l in stagnant water. The fish appeared to become tranquilized in one to three minutes exhibiting no response to external stimulus. Surviving fish, if placed in fresh water, fully recover.

2.3.2 Birds - Deet had teratogenic and embryotoxic effects in white leghorn chicken embryos when 1.27 micromoles of deet were applied to the chorio-allantoic membrane at various times during the second incubation day. Forty-one percent of embryos survived and of these thirty-three percent exhibited gross malformations. Cardiovascular, musculoskeletal and CNS defects were common.

2.3.3 Other species - No information.

3.0 FOR REGULATORY AUTHORITIES - RECOMMENDATIONS ON REGULATION OF COMPOUND

3.1 RECOMMENDED RESTRICTIONS ON AVAILABILITY - (For definitions of categories, see Introduction). All liquid formulation above 10%, and solid formulations above 40%, category 4. All other formulations, category 5.

3.2 TRANSPORT AND STORAGE

Formulations in category 4 - Should be transported and stored in clearly labelled, rigid and leakproof containers, secure from access by children and other unauthorized persons. No food or drink should be transported or stored in the same compartment.

Formulations in category 5 - Should be transported and stored in clearly labelled leakproof containers out of reach of children, away from food and drink.

3.3 HANDLING

Formulations in category 4 - Skin protection (see 4.1.3) should be used by all persons handling the concentrate for prolonged or repeated time periods. Adequate washing facilities should be available at all times during the handling and should be close to the site of handling. Eating, drinking and smoking should be prohibited during handling and before washing of hands and face.

Formulations in category 5 - No facilities other than those needed for the handling of any other chemical are required.

3.4 DISPOSAL AND/OR DECONTAMINATION OF CONTAINER

Containers may be decontaminated prior to disposal. Decontaminated containers should not be used for storage of food or drink. If not decontaminated, large empty containers should be crushed and buried below topsoil. Care must be taken to avoid subsequent contamination of water resources.

3.5 SELECTION, TRAINING AND MEDICAL SUPERVISION OF WORKERS

Formulations in category 4 - Pre-employment medical examination of workers is desirable. Workers suffering from active hepatic or renal disease or dermatitis should be excluded from contact. Special account should be taken of workers' mental ability to comprehend and follow instructions. Training of workers in techniques to avoid contact is advisable.

Formulations in category 5 - No pre-employment medical examination for workers is necessary. Warning to workers to minimize skin contact is essential.

3.6 ADDITIONAL REGULATIONS RECOMMENDED IF DISTRIBUTED BY AIRCRAFT - Not applicable.

3.7 LABELLING

Formulations in category 4 - Minimum cautionary statement

Deet is a substituted toluamide of low mammalian toxicity and should not be used by people under medical advice not to work with such compounds. Avoid all eye contact, mouth contact, excessive skin contact or inhalation of aerosol mist. Wash splashes from skin and eyes immediately. Wash hands before eating or smoking after handling the pesticide.

Do not contaminate food and animal feedstuffs, food preparation surfaces or utensils.

Store pesticide in the original container, tightly closed and in a safe place away from children. Dispose of empty container safely. Do not contaminate ponds, waterways, ditches or ground water with either the chemical directly or the used container.

Avoid prolonged use on children and do not apply to areas of deep skin folds. If signs of poisoning occur after overexposure, take the patient to a physician.

Formulations in category 5 - minimum cautionary statement -

This formulation contains deet. Avoid all eye, mouth and excessive skin contact, or inhalation of the spray mist. Wash hands after use. Store in the original container in a safe place away from children and pets. Avoid prolonged use on children and do not apply to areas of deep skin folds. In addition, for aerosol preparations do not apply directly to face as a spray. Keep container away from heat (including sun). Do not puncture or incinerate aerosol cans even when empty. Dispose of all empty containers safely. Do not contaminate food, food utensils or food preparation surfaces.

3.8 RESIDUES IN FOOD - Not applicable.

4.0 PREVENTION OF POISONING IN MAN AND EMERGENCY AID

4.1 PRECAUTIONS IN USE

4.1.1 General - Deet is a substituted toluamide insect repellent of moderate mammalian toxicity.

4.1.2 Manufacture and formulation - T.L.V.: No information. Closed systems and forced ventilation may be required to reduce as much as possible the exposure of workers to the chemical.

4.1.3 Mixers - When opening the container and when mixing, care should be taken to avoid contact with the skin, mouth and eyes. If necessary, a facial visor and gloves should be worn. Splashes should be washed immediately from the skin or eyes with large quantities of water. Before eating, drinking or smoking, hands and exposed skin should be washed. If contaminated, clothing should be washed at the end of a working day.

4.1.4 Other associated workers - All persons exposed to the concentrate should observe the precautions described above in 4.1.3 under "Mixers and applicators".

4.1.5 Other populations likely to be affected - With recommended usage the general population should not be exposed to hazardous amounts of deet. Caution should be exercised when children are treated for prolonged periods.

4.2 ENTRY OF PERSONS INTO TREATED AREAS - Not applicable.

4.3 DECONTAMINATION OF SPILLAGE AND CONTAINERS - Residues in large concentrate containers should be emptied in diluted form into a shallow pit taking care to avoid contamination of groundwaters. The empty containers may be decontaminated by rinsing two or three times with water and scrubbing the sides. An additional rinse should be carried out with a 5% sodium hydroxide solution which should remain in the container overnight. Impermeable gauntlets should be worn during the work and soakage pit should be provided for the rinsings. Decontaminated containers should not be used for storage of food and drink. Spillage of deet and its formulations should be removed by washing with 5% sodium hydroxide solution and then rinsing with large quantities of water.

4.4 EMERGENCY AID

4.4.1 Early symptoms of poisoning - Symptoms of early systemic poisoning may include respiratory difficulty, confusion, abnormal reflexes and convulsions; ataxia and coma may also occur. Skin contact may result in itchiness, a burning sensation, red patches and blisters on exposed skin surfaces.

4.4.2 Treatment before a person is seen by a physician, if these symptoms appear following exposure - For skin contact, the person should remove contaminated clothing, wash contaminated skin with soap and water and flush with large quantities of water. Vomiting should not be induced following ingestion, inhalation of the solvent must be avoided.

5.0 FOR MEDICAL AND LABORATORY PERSONNEL

5.1 MEDICAL DIAGNOSIS AND TREATMENT IN CASE OF POISONING

5.1.1 General information - Deet is a substituted toluamide insect repellent of slight mammalian toxicity which may be absorbed from the gastrointestinal tract, through the intact skin, and by inhalation.

5.1.2 Symptoms and signs - Symptoms of acute systemic poisoning typical of toxic encephalopathy include respiratory difficulty, shaking spells stimulated by noise or pain, abnormal reflexes, confusion and loss of sense of balance, followed by ataxia and convulsions; coma may also occur. Skin contact may result in hypersteatosis or acute dermatitis, followed in some cases by ulceration in body creases and scarring.

5.1.3 Laboratory - No published information.

5.1.4 Treatment - Treatment is symptomatic. If a potentially lethal dose has been ingested, unless the patient is vomiting, rapid gastric lavage should be performed. For skin contact resulting in toxicity, the skin should be washed with soap and water. If the compound has entered the eyes, they should be washed with isotonic saline or large quantities of water.

5.1.5 Prognosis - If the acute toxic effect is survived and adequate respiratory support was given, the chances of full recovery are good.

5.1.6 References to previously reported cases

1. Gryboski, J., Weinstein, D., Ordway, N. K.
N. Engl. J. Med., 264:289, 1961

2. Heick, H. M. C., Shipman, R. T., Norman, M. G., James, W.
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3. Konovalov, G. A., Ramanov.,
Anesteziol Reanimatol, 2, 54-5, 1980.

4. Maibach, H. I., Johnson, H. L. Arch. Dermatol. 111, 726-30, 1975.

5. PIMS (1980) Summary of Reported Pesticide Incidents Involving Deet.
Pesticide Incident Monitoring System Report No. 365. US EPA 1980.

6. Reuveni, H., Yaqupsky, P. Arch. Dermatol., 118 (8) 582-3, 1982.

7. Zadikoff, C. M. J. Pediatr. 95(1) 140-142, 1979.

5.2 SURVEILLANCE TESTS

Urinary levels of deet and/or metabolites can be used to determine the degree of exposure.

5.3 LABORATORY METHODS

5.3.1 Detection and assay of compound -

Wu, A., Pearson, M. L., Shekoski, D. L., Soto, R. J., Stewart, R. D.,
J. High Resolut. Chromatogr. Chromatog. Commun. 2(9) 558-562, 1979.

5.3.2 Other tests in case of poisoning - No published information.

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