FAO SPECIFICATIONS AND EVALUATIONS FOR PLANT PROTECTION PRODUCTS

DAZOMET

Tetrahydro-3,5-dimethyl-1,3,5-thiadiazine-2-thione

2001

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of plant protection products with the objective that these specifications may be used to provide an international point of reference against which products can be judged either for regulatory purposes or in commercial dealings.

Since 1999 the development of FAO specifications follows the **New Procedure**, described in the 5th edition of the " Manual on the development and use of FAO specifications for plant protection products" (FAO Plant Production and Protection Page No. 149). This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by FAO and the Experts of the "FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent."
FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 2000 onwards the publication of FAO specifications under the **New Procedure** has changed. Every specification consists now of two parts namely the specifications and the evaluation report(s):

Part One: The Specification of the technical material and the related formulations of the plant protection product in accordance with chapter 4, 5 and 6 of the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products".

Part Two: The Evaluation Report(s) of the plant protection product reflecting the evaluation of the data package carried out by FAO and the Panel of Experts. The data are to be provided by the manufacturer(s) according to the requirements of Appendix A, annex 1 or 2 of the "Manual on the development and use of FAO specifications for plant protection products" and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

FAO Specifications under the **New Procedure** do not necessarily apply to nominally similar products of other manufacturer(s), nor to those where the active ingredient is produced by other methods of synthesis. FAO has the possibility to extend the scope of the specifications to similar products, but only when the Panel of Experts has been satisfied that the additional products are equivalent to those which formed the basis of the reference specification.

* Footnote: The publications are available on the Internet under (http://www.fao.org/AG/AGP/AGPP/Pesticid/) or as hardcopy from the Plant Protection Information Officer.

PART ONE

SPECIFICATIONS

DAZOMET

FAO SPECIFICATIONS AND EVALUATIONS FOR
PLANT PROTECTION PRODUCTS

DAZOMET

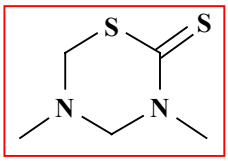
INFORMATION

ISO common name
dazomet (E-ISO, F-ISO [m])

Synonyms
dazomet (BSI, WSSA, JMAF)
tiazon (former USSR)
DMTT (former WSSA name)

Chemical names
IUPAC tetrahydo-3,5-dimethyl-1,3,5-thiadiazine-2-thione
CA tetrahydro-3,5-dimethyl -2*H*-1,3,5-thiadiazine-2-thione

Structural formula



Molecular formula
$C_5H_{10}N_2S_2$

Relative molecular mass
162.3

CAS Registry number
533-74-4

CIPAC number
146

EINECS number
208-576-7

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DAZOMET TECHNICAL MATERIAL

FAO Specification 146/TC (2001)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (146/2001). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (146/2001) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of dazomet together with related manufacturing impurities and shall be an off-white to yellowish solid of sulphurous odour, free from visible extraneous matter and added modifying agents, except a stabilizer (Note 1).

2 Active ingredient

2.1 **Identity tests** (146/TC/(M)/-, CIPAC J, page 38)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Dazomet content** (146/TC/(M)/-, CIPAC J, pages 38-40)

The dazomet content shall be declared (not less than 940 g/kg) and, when determined, the mean measured content shall not be lower than the declared minimum content.

Note 1 A stabilizer is to maintain flow characteristics by preventing the formation of lumps.

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DAZOMET MICROGRANULES

FAO Specification 146/MG (2001)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (146/2001). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (146/2001) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of microgranules containing technical dazomet complying with the requirements of FAO specification 146/TC, together with suitable carriers and any other necessary formulants. It shall be dry, free from visible extraneous matter and hard lumps, free-flowing, essentially non-dusty and intended for application by machine.

2 Active ingredient

2.1 **Identity tests** (146/GR/(M)/-, CIPAC J, page 38)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Dazomet content** (146/GR/(M)/-, CIPAC J, pages 38-42)

The dazomet content shall be declared (g/kg) and, when determined, the mean measured content shall not differ from that declared by more than the following tolerance:

Declared content in g/kg	Tolerance
Above 500	± 25 g/kg

3 Physical properties

3.1 **Nominal size range:** (MT 170, CIPAC F, p. 420)

Not less than 850 g/kg of the formulation shall be within the size range 100-600 µm.

3.2 **Dustiness:** (MT 171, CIPAC F, p. 425, gravimetric)

Essentially non-dusty.

3.3 **Attrition resistance**: (MT 178, CIPAC H, p. 304)

Minimum: 90 % attrition resistance.

4. **Storage stability**

4.1 **Stability at elevated temperature:** (MT 46.3, CIPAC J, p. 128)

After storage at 54 ± 2 °C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage and the formulation shall continue to comply with the clauses for nominal size range (3.1), dustiness (3.2) and attrition resistance (3.3).

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PART TWO

EVALUATION REPORT(S)

DAZOMET

2001 Evaluation report based on submission of data from BASF AG. (TC, MG)

FAO SPECIFICATIONS AND EVALUATIONS FOR
PLANT PROTECTION PRODUCTS

DAZOMET

EVALUATION REPORT 146/2001

Explanation

The data for dazomet were evaluated in support of new FAO specifications.

Dazomet is under patent in many countries in Europe until 2012.

Dazomet was evaluated by the BBA (Germany) in 1971 and reviewed in 1993. It is currently under re-evaluation by the European Commission according to Commission Regulation (EC) No. 451/2000 (List 3).

The draft specification and supporting data were provided by BASF AG in 2001.

Uses

Dazomet is applied before the planting of crops by soil incorporation, thereby causing it to act as a soil fumigant and disinfectant by decomposing to methyl isothiocyanate. It controls soil fungi (i.e. *Fusarium*, *Pythium*, *Rhizoctonia*, *Sclerotinia*, *Verticillium* and *Colletotrichum coccodes (atramentarium)*, nematodes, germinating weed seeds and soil-dwelling insects (Pesticide Manual 2000).

Identity of the active ingredient

ISO common name
dazomet (E-ISO, (*m*)F-ISO)

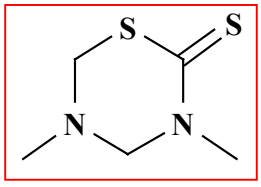
Chemical name(s)
IUPAC
tetrahydro-3,5-dimethyl-1,3,5-thiadiazine-2-thione
CA
tetrahydro-3,5-dimethyl -2*H*-1,3,5-thiadiazine-2-thione

Synonyms
dazomet (BSI, JMAF, WSSA)

tiazon (former USSR)

DMTT (former WSSA name)

Structural formula



Molecular formula

$C_5H_{10}N_2S_2$

Relative molecular mass

162.3

CAS Registry number

533-74-4

CIPAC number

146

EINECS number

208-576-7

Identity tests

The HPLC retention time of dazomet in the sample solution should not deviate by more than 10 s from that of authentic dazomet in the calibration solution (146/TC/(M)/-, CIPAC J, page 38). IR and TLC form additional identity tests.

Physico-chemical properties of pure dazomet (*Table 1*)

Parameter	Value(s) and conditions	Purity %	Method reference
Vapour pressure	5.8 x 10-6 Pa at 20 °C (extrapolated)	>99.5	OECD 104
Melting point and temperature of decomposition	Melting point: 103.2 –105.2 °C Decomposition temperature: 176 °C (with gas evolution)	99.8	OECD 102.
Solubility in water	3.5 g/l at 20 °C at pH 5, pH 7and pH 9	99.8	EEC A6
Octanol/water partition coefficient	log P_{OW} = 0.63 at 20 °C	99.9	EEC A9 OECD Guideline 107, OECD Guideline 117, HPLC method
Hydrolysis characteristics	Half-life = 6 -10 h at pH 5 at 25 °C Half-life = 2 - 3.9 h at pH 7 at 25 °C Half-life = 0.8 - 1 h at pH 9 at 25 °C	radio-chemical purity >95 %	US-EPA Assessment Guidelines, Subdiv.N; § 161-1 (1982)
Photolysis characteristics	t_{50} = 4.2 h t_{50} = 7.8 h for dark control solution xenon arc source, 150 Klux, λ >290 nm, temperature = 25°C, pH 5	radio-chemical purity > 95 %	US-EPA Assessment Guidelines, Subdiv.N; § 161-2 (1982)
Dissociation characteristics	Does not dissociate.	99.9	OECD 112, titration method

Chemical composition and properties of dazomet technical material (TC) (*Table 2*)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information was supplied and is held on file by FAO. Mass balances were 100.0 to 100.2% and no unknowns were detected.
Declared minimum [a.i.] content	940 g/kg
Relevant impurities **≥** 1 g/kg and maximum limits for them	None
Relevant impurities **<** 1 g/kg and maximum limits for them:	None
Stabilisers or other additives and maximum limits for them:	A stabilizer is required to avoid the formation of lumps. It was not identified but the maximum concentration was stated to be 50 g/kg.
Melting temperature range of the TC	103.2 – 105.2 °C

Hazard summary

Notes.

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from dazomet having impurity profiles similar to those referred to in the table above.

(ii) The conclusions expressed in the summary below are those of the proposer, unless otherwise specified.

Table 3. Toxicology profile of the dazomet technical material, based on acute toxicity, irritation and sensitization.

Species	Test	Duration and conditions or guideline adopted	Result (dazomet)
Rat (m f)	Oral	14 days, guideline not specified	LD_{50} = 415 mg/kg bw
Rat (m f)	Dermal	EPA/FIFRA; OECD, EEC	LD_{50} > 2000 mg/kg bw
Rat (m f)	Inhalation	EPA/FIFRA; OECD (403)	LC_{50} = 8400 mg/m^3
Rabbit (m f)	Skin irritation	EPA/FIFRA; OECD (404)	Non-irritant
Rabbit (m f)	Eye irritation	EPA/FIFRA; OECD; EC (8.3/467/EEC)	Non-irritant
Guinea pig (f)	Skin sensitization	EPA/FIFRA; OECD (406)	Non-sensitizing

Dazomet is of moderate acute oral toxicity but of low dermal and inhalation toxicity. It was not irritating to skin and eyes and showed no skin-sensitizing properties.

Table 4. Toxicology profile of the technical material based on repeated administration (sub-acute to chronic)

Species	Test	Duration and conditions or guideline adopted	Result
Rat (m f)	Oral	90 d; EPA (F § 82-1, 66-76, NTIS) OECD (408), Japan MAFF (1982)	NOAEL = 1.5 mg/kg bw/d
Rabbit (m f)	Dermal	21 d; EPA/FIFRA (F§82-2)	NOAEL = 1000 mg/kg bw/d
Rat (m f)	Inhalation	28 d, not specified	NOAEL = 5 mg/m³
Mouse (m f)	Carcinogenicity (feeding)	18 mo ; EPA (F, § 83-2, 117-125, NTIS), OECD (451), Japan MAFF (1985)	Not carcinogenic
Rat (m f)	Carcinogenicity (feeding)	24 mo, EPA (F § 83-2, 107–117, NTIS); OECD (452), Japan MAFF (1985)	Not carcinogenic
Dog (m f)	Oral toxicity	3 mo; EPA (F § 82-1, 66 – 76, NTIS , OECD (409), Japan MAFF (1985)	NOEL = 23-25 mg/kg bw/d
Dog (m f)	Oral toxicity (feeding)	12 mo, EPA (F § 83-1, 107 –117, NTIS), OECD (452), Japan MAFF (1985)	NOAEL = 1 mg/kg bw/d
Rat (m f)	Reproduction (feeding)	2 generation EPA/FIFRA (F § 83-4, NTIS), OECD (416), Japan MAFF (1985)	NOAEL(reproduction) = 18 mg/kg bw/d NOAEL (systemic tox) = 0.49 mg/kg bw/d (F0 + F1) NOAEL (systemic tox) = 18 mg/kg bw/d (F1ab + F2)
Rat (f)	Teratogenicity	EPA/FIFRA (F § 83-3), OECD (414), Japan MAFF (1985)	Not teratogenic NOAEL = 3 mg/kg bw/d
Rabbit (f)	Prenatal toxicity (feeding)	(EPA/FIFRA (F § 83-3, 126-130, NTIS) OECD (414), EC Commission Directive 87/ 302/ EEC, Japan MAFF(1985)	Not teratogenic NOAEL = 15 mg/kg bw/d

Animal studies have shown that dazomet can cause damage to the liver when it is administered repeatedly and in high doses. Clear thresholds of effect could be determined.

In long-term studies, no carcinogenicity was found. Animal studies did not show any indication of developmental toxicity or impairment of fertility.

Table 5. Mutagenicity profile of the technical material based on in vitro and in vivo tests

Species	Test	Conditions	Result
Bacillus subtilis	Mutagenicity*, in vitro*	24-48 h incubation	Not mutagenic
CHO cells (HGPRT locus)	Point mutation	Dose range: 0.01-0.464 µg/ml with and without metabolic activation system (S9 mix) made of Sprague-Dawley rat liver	Mutagenic
Human lymphocytes	Cytogenetic investigations, *in vitro*	OECD (473)	Not clastogenic
Balb/3T3 cells	Mutagenicity, in vitro	Dose range: 0.078 µg/ml – 1.25 µg/ml, incubation with Balb/3T3 cells for 72 h (37 °C)	Not cytotoxic No morphological transformation
Rat hepatocyte	Unscheduled DNA synthesis, *in vivo* and *in vitro*	Dose range: 300 mg/kg – 37.5 mg/kg. The hepatocytes were isolated 4 h after oral gavage.	Inactive
Rat bone marrow	Mutagenicity, potential activity to cells arrested at metaphase of mitosis	Doses: ½ LD_{50} , ⅓ LD_{50}, 1/10 LD_{50} and 5 mg/kg, 6 rats at each concentration. Acute (single dose) and sub-chronic (5 consecutive doses).	Not clastogenic No effect on the mitotic process

Dazomet did not show any mutagenic properties in various tests (*in vivo* and *in vitro*

Table 6. Ecotoxicology profile of the technical material

Species	Test	Duration and conditions	Result
Daphnia magna (water flea)]	acute toxicity	48 h, static water	EC_{50} = 0.3 mg/l NOEC = 0.1 mg/l
Salmo gairdneri (rainbow trout)	Acute toxicity	96 h, static water	LC_{50} = 0.16 mg/l
Oncorhynchus mykiss (rainbow trout)	Acute toxicity	96 h, flow through EPA/FIFRA (72-1)	LC_{50} = 25 mg/l NOEC = 1.0 mg/l
Lepomis macrochirus (bluegill sunfish)	Acute toxicity	96 h, static water	LC_{50} = 0.3 mg/l
Lepomis macrochirus (bluegill sunfish)	Acute toxicity	96 h, flow through EPA/FIFRA (72-1)	LC_{50} = 79 mg/l NOEC = 26 mg/l
Ankistrodesmus bribaianus (green alga)	Acute toxicity	72 h, static water	EC_{50} = 1.08 mg/l
Colinus virginianus (Bobwhite quail)	acute toxicity	21 d	LD_{50} = 415 mg/kg bw
Colinus virginianus (Bobwhite quail)	dietary toxicity	8 d	LC_{50} = 1850 mg/kg food
Anas platyrhynchos (Mallard duck)	dietary toxicity	8 d	LC_{50} > 5000 mg/kg food
Colinus virginianus (Bobwhite quail)	Reproductive toxicity	25 weeks OECD (206), EPA (E § 71-4), SEP/ FDA 540-9-86-139	NOEL = 100 mg/kg food
Apis mellifera (Honey bee)	Acute oral and contact	Stevenson 1978 (no details given)	LD_{50} oral = >10 µg/bee LD_{50} contact = >50 µg/bee

The ecotoxicological effects of dazomet were investigated using various organisms from major ecotoxicological groups. The results demonstrated that dazomet is very toxic to aquatic organisms like fish, crustaceans and algae, and moderately toxic to birds. Due to the mode of application, which prevents exposure to bees, the product was rated as harmless to bees.

Dazomet has not been evaluated by the FAO/WHO JMPR or in the Environmental Health Criteria series, but has been classified by IPCS by hazard as slightly hazardous, class III, and noted as being irritant to skin and eyes (WHO 2002; ICSC 786).

Formulations and co-formulated active ingredients

The main formulation type available is of micro granules (MG). The most common trade mark is “Basamid Granular”. Different names are used in some countries. The formulations are registered and sold in many countries throughout the world.

Dazomet is not co-formulated with other pesticides.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is a full CIPAC method (CIPAC Handbook J, pages 37-42, 2001). Dazomet is determined by reversed phase HPLC (C_{18}, acetonitrile/water/acetic acid), using UV detection at 284 nm and external standardization.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD, EU or USEPA, while those for the formulation were CIPAC (nominal size range, MT 170; dustiness, MT 171 gravimetric; attrition resistance, MT 178; accelerated stability, MT 46), as indicated in the specifications.

Physical properties

The physical properties, the methods for testing them and the limits proposed for the MG formulations, comply with the requirements of the FAO Manual (5th edition).

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as dazomet, in g/kg.

Appraisal

The data for dazomet were submitted by the proposer in accordance with the requirements of the FAO Manual (5th edition), and evaluated in support of the new FAO specifications.

The production of dazomet is under patent in many countries in Europe, until 2012. Dazomet was evaluated by the BBA (Germany) in 1971 and reviewed in 1993. It is currently under re-evaluation by the European Commission, according to Commission Regulation (EC) No. 451/2000 (List 3).

Dazomet is an off-white to yellowish solid of sulphurous odour. It melts in the range 103 to 105°C and is of low water solubility (3.5 g/l). It is formulated as microgranules (MG) known as “Basamid Granular”. Dazomet rapidly hydrolyses in water, the rate increasing with increasing pH, and is relatively prone to photodegradation.

The proposer provided the meeting with commercially confidential information on the manufacturing process and batch analysis data. Impurities were identified at or above 1 g/kg and manufacturing limits were specified for them. The meeting considered none of them to be relevant.

Particular consideration must be given to the rapid decomposition of dazomet when it comes in contact with water or humid air, generating gaseous methyl isothiocyanate (MITC). However, the proposer has indicated that the

determination of the physico-chemical properties of pure dazomet (Table 1) such as solubility in water, the octanol/water partition coefficient (Pow), and photolysis charactersitics, could be clearly attributed to only dazomet and not to both dazomet and MITC.

Concerning the toxicology and ecotoxicology data (Table 3-6), the proposer has indicated that these data were attributed to dazomet irrespective of whether MITC was generated or not. However, this evaluation must identify the fact that certain conflicting assessments may have arisen from the difficulty of assessing dazomet characteristics when methyl isothiocyanate is almost inevitably generated under the conditions of test. In other words, the toxicology/ecotoxicology data refer to dosing with dazomet, and the observed effects may have been caused by dazomet, MITC or both. The Meeting recognised that apart from conducting parallel studies with dazomet and MITC, there is no way to distinguish between their effects. For instance, the Proposer's assessment is that dazomet technical material is not irritating to the skin and eyes, and shows no skin-sensitising properties (Table 3). This conflicts with the WHO/PCS hazard classification, based on earlier, published studies, which indicates that dazomet is an irritant to skin and eyes. Recent case reports also indicate that dazomet may have low sensitizing potential to skin in humans.

The irritancy of methyl isothiocyanate is well known and it may have been responsible for the effects observed. Nonetheless, the generation of methyl isothiocyanate from dazomet cannot be avoided under the conditions. Thus there is an underlying difficulty in separating 'dazomet data' from 'methyl isothiocyanate data'. This difficulty is due to the differing and potentially unpredictable degrees of dazomet decomposition that occurs in different aqueous environments. Thus, wherever water is present during any particular test, some doubt must remain as to whether the measurement recorded was due to the presence of dazomet and/or to its daughter compound methyl isothiocyanate. Taking into account this problem of data interpretation, the meeting accepted the data presented by the proposer.

Dazomet is toxic to aquatic organisms like fish, crustaceans and algae, and is moderately toxic to birds.

An additive is required to assist in flow characteristics of the hygroscopic dazomet TC. Although a stabilizer is usually added to a TC to ensure chemical stability of the active ingredient, in this case the additive could be considered to be a physical stabilizer. The term, stabilizer, is not defined in the FAO Manual, but stabilizers are the only additives recognised in TC specifications. The meeting agreed that the additive could be considered as a stabilizer in this case. The meeting concluded that confidentiality of the identity of a stabilizer in the TC should be addressed in the revision of the Manual. The concentration of a stabilizer is supposed to be identified in a note to the specification but it is difficult or impossible for the purchaser to check the concentration of an unidentified component.

The proposer declared that dazomet produced and commercialised by BASF complies with the FAO specifications (2001).

Recommendation

The meeting recommended that the specifications for dazomet TC and MG, presented by BASF AG, should be adopted as FAO specifications.

References

Pesticide Manual	The Pesticide Manual , 12th Edition, British Crop Protection Council, 2000, UK.
CIPAC F	Handbook F, Collaborative International Pesticides Analytical Council, 1995, UK
CIPAC H	CIPAC Handbook H, Collaborative International Pesticides Analytical Council, 1998, UK
CIPAC J	CIPAC Handbook J, Collaborative International Pesticides Analytical Council, 2001, UK
FAO Manual	Manual on the development and use of FAO specifications for plant protection products, 5th edition. FAO Plant production and protection paper 149. FAO, 1999, Rome.