FAO SPECIFICATIONS AND EVALUATIONS

FOR PLANT PROTECTION PRODUCTS

METAZACHLOR

2-chloro-*N*-(pyrazol-1-ylmethyl)acet-2',6'-xylidide

1999

Food and Agriculture Organization
of the United Nations

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INTRODUCTION

FAO establishes and publishes specifications* for technical pesticides 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 has followed 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 required for evaluation, the procedures to be applied in the evaluation process 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 the products of manufacturers whose data have been evaluated as satisfactory and to whose products the specifications are thus known to be appropriate. Consequently from the year 2000 onwards the publication of FAO specifications under the **New Procedure** has changed. Every specification document consists now of two parts, namely the specifications and the evaluation report(s):

Part One: The Specifications of the technical material and the related formulations of the plant protection product, in accordance with the requirements of chapters 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, and providing the justification for any deviation in the specifications from requirements of the 5th edition of the Manual. The data have been provided by the manufacturer(s) according to the requirements of Appendix A, Annex 1, of the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products". The Evaluation Report includes the name(s) of the manufacturer(s) whose technical pesticide has been evaluated.

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 may extend the scope of the specifications to notionally similar products, if 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/waicent/faoinfo/agricult/agp/) or as hardcopy from the Plant Protection Information Officer.

FAO SPECIFICATIONS AND EVALUATIONS FOR PLANT PROTECTION PRODUCTS

METAZACHLOR SPECIFICATIONS

411/TC (1999)

INFORMATION

ISO common names

metazachlor (BSI, E-ISO)

metazachlore ((m) F-ISO)

Chemical names

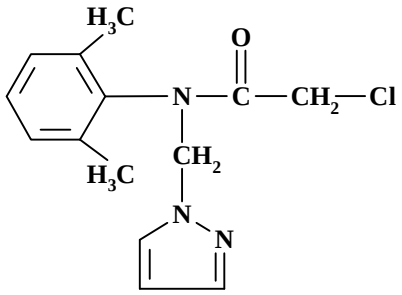
IUPAC

2-chloro-*N*-(pyrazol-1-ylmethyl)acet-2',6'-xylidide

CA

2-chloro-*N*-(2,6-dimethylphenyl)-*N*-(1*H*-pyrazol-1-ylmethyl)acetamide

Structural formula



Molecular formula

$C_{14}H_{16}ClN_3O$

Relative molecular mass

277.8

CAS Registry number

67129-08-2

CIPAC number

411

EINECS number

266-583-0

METAZACHLOR TECHNICAL

411/TC (1999)

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 (411/1999). 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 (411/1999) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of metazachlor together with related manufacturing impurities and shall be a beige solid free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (411/TC/M/2, CIPAC E, p. 135)

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

2.2 **Metazachlor content** (411/TC/M/3, CIPAC E, p. 135)

The metazachlor 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.

METAZACHLOR AQUEOUS SUSPENSION CONCENTRATES

411/SC (1999)

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 (411/1999). 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 (411/1999) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical metazachlor, complying with the requirements of FAO specification 411/TC (1999), in an aqueous phase together with suitable formulants. After agitation the material shall be homogeneous (Note 1) and suitable for further dilution in water.

2 Active ingredient

2.1 **Identity tests** (411/SC/M/2, CIPAC E, p. 137)

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

2.2 **Metazachlor content** (411/SC/M/3, CIPAC E, p. 138)

The metazachlor content shall be declared (g/l at 20°C or g/kg) (Note 2) and, when determined, the mean measured content shall not differ from that declared by more than the following amounts:

Declared content in g/kg or g/l at 20 °C	Tolerance
above 100 up to 250	± 6% of the declared content
above 250 up to 500	± 5% of the declared content
above 500	± 25 g/l
Note In each range the upper limit is included	

3 Physical properties

3.1 **Mass per millilitre** (MT 3.3.2, CIPAC F, p. 19)

The mass per millilitre (g/ml) at 20 ± 2 °C shall be declared.

3.2 **pH range** (MT 75.2, CIPAC F, p. 206)

pH range: 5.0 to 8.0

3.3 **Pourability** (MT 148, CIPAC F, p. 348)

Maximum "residue": 9.0 %

3.4 **Spontaneity of dispersion** (MT 160, CIPAC F, p. 391) (Note 3)

A minimum of 75 % of the metazachlor content found under 2.2 shall be in suspension after 5 min in CIPAC Standard Water D at 30 ± 2°C (Note 4).

3.5 **Suspensibility** (MT 161, CIPAC F, p. 394) (Note 3)

A minimum of 75 % of the metazachlor content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2°C (Note 4).

3.6 **Wet sieve test** (MT 59.3 CIPAC F, p. 179)

Maximum: 1.0 % of the formulation shall be retained on a 75 µm test sieve.

3.7 **Persistent foam** (MT 47.2. CIPAC F, p. 152) (Note 5)

Maximum: 20 ml after 1 min.

4 Storage stability

4.1 **Stability at 0°C** (MT 39, CIPAC F, p. 128)

After storage at 0 ± 2°C for 7 days, the formulation shall continue to comply with suspensibility (3.5) and wet sieve test (3.6).

4.2 **Stability at elevated temperature** (MT 46 CIPAC F, p. 148)

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 (Note 6) and the product shall continue to comply with the clauses for pH range (3.2), pourability (3.3), spontaneity of dispersion (3.4), suspensibility (3.5) and wet sieve test (3.6), as required.

Note 1 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or of sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example by inverting the closed container several times). Large containers must be opened and stirred adequately. After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer "cake" is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a laboratory sample taken after the recommended homogenization procedure.

Note 2 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and in calculation of the active ingredient content in (g/l) if methods other than MT 3.3 are used. If the buyer requires both g/kg and g/l at 20°C then, in case of dispute the analytical results shall be calculated as g/kg.

Note 3 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis provided that these methods have been shown to give results equal to those of the chemical assay method. In case of dispute, the chemical method shall be the referee method.

Note 4 Unless other temperatures and/or times are specified.

Note 5 The mass of sample to be used in the test should be specified at the application rate of use recommended by the supplier.

Note 6 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

FAO SPECIFICATIONS AND EVALUATIONS FOR PLANT PROTECTION PRODUCTS

METAZACHLOR

EVALUATION REPORT 411/1999

Explanation

Metazaclor was a new compound evaluated for FAO specifications under the new procedure adopted in 1999.

Metazachlor had been not evaluated by the JMPR or the IPCS but a draft monograph was being prepared for the European Union.

The proposer of the specifications was BASF AG and the data were provided in 1999.

Uses

Metazachlor formulations are selective herbicides, absorbed by the hypocotyls and roots and inhibiting germination.

The products are used in pre-emergence and early post-emergence control of winter- and annual grasses (e.g. *Alopecurus myosuroides*, *Apera spica-venti*, *Avena fatua*, *Digitalia sanguinalis*, *Echinochloa crus-galli*, *Poa annua* and *Setaria spp*.) and broad-leaved weeds (e.g. *Amaranthus*, *Anthemis*, *Matricaria*, *Polygonum*, *Sinapis*, *Solanum*, *Stellaria*, *Urtica* and *Veronica spp*.) in artichokes, broccoli, asparagus, Brussels sprouts, cabbages, cauliflowers, sweetcorn, garlic, horseradish, kale, leeks, maize, white mustard, onions, peanuts, pome fruits, potatoes, radish, rape, soya beans, stone fruits, strawberries, sugar cane, sunflowers, tobacco and turnips. (Pesticide Manual, 1997).

Identity

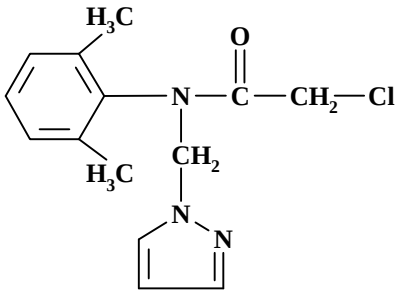
ISO Common names:

metazachlor (BSI, E-ISO)
metazachlore ((m) F-ISO)

Chemical names

IUPAC:
2-chloro-*N*-(pyrazol-1-ylmethyl)acet-2',6'-xylidide
CA:
2-chloro-*N*-(2,6-dimethylphenyl)-*N*-(1*H*-pyrazol-1-ylmethyl)acetamide

Structural formula:



Molecular formula:

$C_{14}H_{16}ClN_3O$

Relative molecular mass:

277.8

CAS Registry number:

67129-08-2

CIPAC number:

411

EEC number:

266-583-0

Identity tests:

The test relies on the HPLC method for metazachlor analysis. The retention time of metazachlor in the sample solution should not deviate by more than 1% from that of authentic metazachlor in the calibration solution (CIPAC E, p. 135). There is also an infra-red test (CIPAC E, p. 135).

Physico-chemical properties of the pure active ingredient

Vapour pressure:	$0.9 \cdot 10^{-4}$ Pa at 20°C. The vapour pressure of pure metazachlor was estimated by extrapolation
Melting points:	Melting points different according to the solvent from which crystals are obtained - pproximately 85°C for pure metazachlor crystallized from cyclohexane, approximately 80°C from chloroform/hexane, approximately 76°C from diisopropyl ether
Temperature of decomposition:	Pure metazachlor:approximately 205°C, with gas evolution
Solubility in water:	Pure metazachlor: 450 mg/l (20°C)
Octanol / water partition coefficient:	log P_{ow} = 2.49
Hydrolysis characteristics:	At pH 5,7 and 9, and at 22°C, metazachlor exhibited hydrolytic half-lives of 766, 670 and 487 days in aqueous solutions, respectively. Due the very slow rate of hydrolysis, metazachlor is considered stable in suspension concentrates under normal conditions.

Chemical composition and properties of the technical material (TC)

The meeting was provided with commercially confidential information on the manufacturing process and on the impurities present at or above 1 g/kg.

Declared minimum active ingredient content in the technical material:

940 g/kg

Relevant impurities and maximum limits for them:

none of the impurities reported at or above 1 g/kg in the analytical profile of the batches was considered relevant and no known relevant impurities likely to be present <1 g/kg.

Hazard summary

Toxicological profile of the technical material based on acute oral, dermal and inhalation toxicity, skin and eye irritation and skin sensitisation

Acute studies

Species	Test	Result obtained
Rat	Oral LD_{50}	2150 mg/kg
Rat	Inhalation LC_{50}	> 34.5 mg/l (4 h)
Rat	Dermal LD_{50}	> 6810 mg/kg
Mouse	Oral LD_{50}	2010 mg/kg
Rabbit	Skin irritancy	not irritating
Rabbit	Eye irritancy	not irritating
Guinea Pig	Skin sensitisation	sensitizing

The purity of the test material was not reported.

Metazachlor has a low acute oral, dermal, and inhalation toxicity. It was not irritating to skin and eye. Metazachlor showed skin sensitising properties.

Toxicological profile of the technical material based on repeated administration (from sub-acute to chronic) and studies such as developmental toxicity, genotoxicity, carcinogenicity, etc.

Species	Study Type	Results Obtained
Rat	90-day toxicity	1200 ppm (≡ 100 mg/kg bw)
Dog	26-week toxicity	200 ppm (≡ 8 mg/kg bw)
Rat	2-year toxicity and carcinogenicity	100 ppm (≡ 3.5 mg/kg bw)
Mouse	2 year carcinogenicity	200 ppm (≡ 20 mg/kg bw)
Rat	Reproduction	>1000 ppm (≡ 80 mg/kg bw)
Rat	Teratogenicity Maternal toxicity Developmental toxicity	 150 mg/kg bw 450 mg/kg bw
Rabbit	Teratogenicity Maternal toxicity Developmental toxicity	 250 mg/kg bw

The purity of the test material was not reported.

Animal studies have shown that metazachlor can cause damage to the liver, kidneys and blood count when it is administered repeatedly orally in high doses. Clear thresholds could be determined.

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

Metazachlor did not show any mutagenic properties in various test systems (*in vitro* and *in vivo*).

ADI calculation: 0-0.036 mg/kg bw, corresponding to 0-2.52 mg/person/day for a 70 kg person.

Genotoxicity

In vitro mutagenicity studies			
Test System	Target Cells	Medium	Result
Bacterial Mutation Assay	Salmonella typhimurium TA98, TA 100, TA1535, TA1537,	with and without S-9 mix	negative
Mammalian cell gene mutation assay	Chinese hamster V 79 cells	with and without S-9 mix	negative
Mammalian cell cytogenetic assay	CHO cells	with and without S-9 mix	negative

In vivo mutagenicity studies		
Test System	Target	Result
Sister chromatid exchange (SCE)	Chinese hamster	negative

The purity of the metazachlor used was not stated.

Ecotoxicological profile

Species	Test	Result obtained

Daphnia magna (waterflea)	EC_{50} (48 h)	22.3 mg/l
Daphnia magna (waterflea) reproduction	NOEC (21 d)	6.25 mg/l
Salmo gairdneri (rainbow trout)	LC_{50} (96 h)	4.0 mg/l
Salmo gairdneri (rainbow trout)	NOEC (28 d)	2.15 mg/l
Lepomis macrochirus (bluegill sunfish)	LC_{50} (96 h)	15 mg/l
Cyprinus carpio (carp)	LC_{50} (96 h)	15 mg/l
Chlorella (green alga)	EC_{50} (96 h)	1.63 mg/l
Ankistrodesmus bibraianus	EC_{50} (72 h)	9.6 mg/l
Pseudokirchneriella subcapitata	EC_{50} (72 h)	0.031 mg/l
Colinus virginianus (quail)	acute LD_{50}	>2000 mg/kg bw
Colinus virginianus (quail)	short-term (8 d) LC_{50}	>5620 mg/kg feed
Anas platyrhynchos (duck)	acute LD_{50}	>250 mg/kg bw
Anas platyrhynchos (duck)	short-term (8 d) LC_{50}	>5620 mg/kg feed
Apis mellifera (honeybee)	LD_{50}	>100 µg/bee
Eisenia fetida (earthworm)	LC_{50} (14 d)	440 mg/kg soil
Soil micro-organisms: Respiration	1x and 5 x rate (28 d)	negligible effects
Soil micro-organisms: Nitrification	1x and 5 x rate (28 d)	negligible effects

The purity of the metazachlor used was not stated.

The ecotoxicological effects of metazachlor were investigated using various organisms from major ecological groups. The results demonstrated that metazachlor is not hazardous to soil microflora, earthworms, birds, honeybees. Metazachlor is moderately toxic to daphnia, carp and bluegill sunfish. The most sensitive species tested were trout and green algae. The octanol/water partition coefficient of metazachlor (log P_{ow} 2.49) precludes bioaccumulation.

Metazachlor has not yet been evaluated by the FAO/WHO JMPR. Metazachlor is classified in table 5 as technical grade active ingredient of pesticides unlikely to present acute hazard in normal use by the WHO Recommended Classification of Pesticides by Hazard (1998/99).

Formulations

Main formulation types in the market:

Metazachlor is usually formulated in suspension concentrates (SCs). The most common trade mark is "Butisan S". Different names are used in some countries, in particular for mixtures with other active ingredients.

Main countries where the formulations are registered and sold:

"Butisan S" and other metazachlor formulations are registered and sold in about 40 countries in Africa, Europe and Asia.

Methods of analysis and testing

Determination of identity and active ingredient content of technical material (TC):

The HPLC retention time is used to determine the identity (RT deviation, maximum 1%) but an IR method is provided as an alternative.

Determination of the active ingredient content in technical materials are based upon CIPAC methods, CIPAC Handbook E: Metazachlor 411 (pp. 135 - 138). The active ingredient is separated by HPLC on a reversed-phase column (C_{18}, methanol/water) and quantitatively determined by UV detection with external standardization.

Determination of relevant impurities:

There are no relevant impurities and therefore no methods are necessary.

Test methods for physical properties of the suspension concentrate (SC):

Mass per millilitre: MT 3.3.2, CIPAC F, p.19
pH range: MT 75.2, CIPAC F, p.206
Pourability: MT 148, CIPAC F, p.348
Spontaneity of dispersion: MT 160, CIPAC F, p.391
Suspensibility: MT 161, CIPAC F, p.394
Wet sieve test: MT 59.3, CIPAC F, p.179
Persistent foam: MT 47.2, CIPAC F, p.152
Storage stability at 0°C: MT 39, CIPAC F, p.128
Storage stability at 54°C: MT 46, CIPAC F, p.148

Physical properties

The proposer declared that metazachlor TC and SC comply with the proposed FAO specifications (1999).

Containers and packaging

Special requirements for containers and packaging:

none identified.

Expression of active ingredient

The active ingredient is expressed as metazachlor, in g/kg (or, alternatively, for SC in g/l). In cases of dispute, the content is expressed as g/kg.

Appraisal

This was the first evaluation of metazachlor for FAO specifications.

Metazachlor and its formulations are registered in many countries throughout the world.

Metazachlor has sparing solubility in water. It is only very slowly hydrolysed in water and is considered stable in suspension concentrates under normal conditions.

The meeting was provided with information on the nature of impurities exceeding 0.1%. None of these impurities is relevant regarding adverse effects on the properties of the product and/or the technical material. A full description of the manufacturing process was provided.

Metazachlor has a low acute oral, dermal and inhalation toxicity. It is not irritating to skin and eyes but shows skin sensitizing properties.

Animal studies have shown that metazachlor can cause damage to the liver, kidneys and blood count when administered repeatedly orally but only at high doses. Clear thresholds could be determined.

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

Metazachlor did not show any mutagenic properties in various test systems (*in vitro* and *in vivo*).

The ecotoxicity of metazachlor was investigated using various organisms from major ecological groups. The results demonstrated that metazachlor is not hazardous to soil microflora, earthworms, birds, honeybees. Metazachlor is moderately toxic to daphnia, carp and bluegill. The most sensitive species tested were trout and green algae. The octanol/water partition coefficient of metazachlor (log P_{ow} 2.49) precludes bioaccumulation.

The calculated ADI is 0-0.036 mg/kg bw, corresponding to 0-2.52 mg/person/day for a 70 kg.

CIPAC methods are available for testing the physical and chemical properties of the technical material (TC) and formulations (SC).

The proposer declared that metazachlor produced and commercialised by BASF complies with the proposed specifications.

Recommendations

The meeting recommended acceptance of the proposed specifications.

It may be appropriate for the FAO/WHO JMPR and WHO IPCS to evaluate the data relating to effects on the liver, kidneys and blood count when metazachlor is administered repeatedly orally at in high doses.

References

FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent. Group of Expert on Pesticide Specifications, 3rd Session, October 1998, Rome.

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CIPAC Handbook E, Black Bear Press Ltd, 1993, UK.

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