



Food and Agriculture Organization
of the United Nations

AGP: CP/219

PROVISIONAL
FAO SPECIFICATIONS
FOR PLANT PROTECTION PRODUCTS

ALDICARB

2-methyl-2-(methylthio) propionaldehyde
O-methylcarbamoyloxime

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
Rome, 1988

Group on Pesticide Specifications

FAO Panel of Experts on Pesticide Specifications, Registration Requirements and
Application Standards

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DISCLAIMER¹

FAO specifications are developed with the basic objective of promoting, as far as practicable, the manufacture, distribution and use of pesticides that meet basic quality requirements.

Compliance with the specifications does not constitute an endorsement or warranty of the fitness of a particular pesticide for a particular purpose, including its suitability for the control of any given pest, or its suitability for use in a particular area. Owing to the complexity of the problems involved, the suitability of pesticides for a particular purpose and the content of the labelling instructions must be decided at the national or provincial level.

Furthermore, pesticides which are manufactured to comply with these specifications are not exempted from any safety regulation or other legal or administrative provision applicable to their manufacture, sale, transportation, storage, handling, preparation and/or use.

FAO disclaims any and all liability for any injury, death, loss, damage or other prejudice of any kind that may arise as a result of, or in connection with, the manufacture, sale, transportation, storage, handling, preparation and/or use of pesticides which are found, or are claimed, to have been manufactured to comply with these specifications.

Additionally, FAO wishes to alert users to the fact that improper storage, handling, preparation and/or use of pesticides can result in either a lowering or complete loss of safety and/or efficacy.

FAO is not responsible, and does not accept any liability, for the testing of pesticides for compliance with the specifications, nor for any methods recommended and/or used for testing compliance. As a result, FAO does not in any way warrant or represent that any pesticide claimed to comply with a FAO specification actually does so.

¹ This disclaimer applies to all specifications published by FAO.

INTRODUCTION TO FAO SPECIFICATIONS DEVELOPED UNDER THE OLD PROCEDURE

Between 1975 and 2000, FAO published booklets of specifications for technical materials and related formulations of plant protection products. Revisions of, and additions to, already published specifications will be issued when necessary. However, all changes and revisions of FAO specifications are now subject to the new procedure described in the *Manual on the development and use of FAO and WHO Specifications for Plant Protection Products*, FAO Plant Production and Protection Paper No. 173, Rome 2002 (*Revised First Edition* available only on the FAO home page of the Internet at: <http://www.fao.org/pest-and-pesticide-management/en/>)

FAO specifications developed under the old procedure are based on the requirements defined in the Fourth Edition of the *Manual on the development and use of FAO specifications for plant protection products*, Plant Production and Protection Paper No. 128, Rome 1995.

This manual contained detailed definitions and other essential background information on basic procedures and technical principles adopted by the group on Pesticide Specifications of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent, such as:

1. Classes of Specifications (page 10 of the Manual).

FAO (full) specifications (Code "S"). Specifications that have all necessary requirements together with CIPAC (full) methods, or other collaboratively studied (proven) methods. 2/ and 3/.

FAO Provisional specifications [Code (S)] are those for which more evidence of the necessary parameters is available and where some collaborative study of the methods of analysis has been carried out.

FAO Tentative specifications (Code "ts") are those which have been recommended by FAO as preliminary specifications which are based on minimum requirements. The methods of analysis cited are normally supplied by the manufacturer or may already have been published or be the subject of collaborative work.

Wherever possible, standards for apparatus and common names for pesticides are those approved by the International Standards Organization (ISO).

2. Expression of Active Ingredient Content (page 18 of the Manual)

- for solids, liquid technical materials, volatile liquids (of maximum boiling point 50°C) and viscous liquids (with minimum kinematic viscosity of $1 \times 10^{-3} \text{ m}^2 / \text{s}$ at 20°C) the FAO Specification shall be based on g/ kg expression of content;

- for all other liquids the active ingredient content of the product shall be declared in terms of g/kg or g/l at 20°C. 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.

3. Tolerance on Content (page 19 of the Manual).

A declared content of active ingredient must be included in all specifications, and one of the problems immediately arising is the level of tolerance acceptable above the nominal figures. The tolerance is influenced by (a) the reproducibility of the method of analysis, (b) the sampling error and (c) the manufacturing variance.

Allowable variations in analytical results (i.e., tolerances in content of active ingredient) with respect to specific pesticide consignments are intended to cover reasonable variations in content of active ingredient. For examples of such permitted tolerances, see the table on page 20 of the Manual.

4. Containers/Packaging (page 32 of the Manual).

Containers shall comply with pertinent national and international transport and safety regulations.

- Technical material, dustable powders and granules

Containers shall be suitable, clean, dry and as specified, and shall not adversely affect, or be affected by, the product/material, but shall adequately protect it against external conditions.

- Wettable Powders

The product shall be packed in suitable, clean, dry containers as specified in the order. The container shall provide all necessary protection against compaction, atmospheric moisture, oxidation, loss by vaporization and/or contamination to ensure that the product suffers no deterioration under normal transit and storage conditions.

The product shall be protected by an adequate moisture barrier. This may be a suitable bag of polyethylene or alternative means of giving equal or better protection.

- Solutions and emulsifiable concentrates

Containers shall be lined, where necessary, with a suitable material, or the interior surfaces treated to prevent corrosion and/or deterioration of the contents.

Additional information should be given in all specifications where particular pesticides present problems in packaging.

5. Biological information (page 33 of the Manual).

- Phytotoxicity

No test can be specified to cover possible phytotoxicity of formulation to all crops. When a crop is not mentioned in the instructions for use, purchasers should check with the supplier that the material is suitable, always provided that such a use is not restricted or legally forbidden.

- Wetting of crops

The dilute spray should satisfactorily wet the leaves of the specified crops when used in accordance with the instructions. Test method MT 53.2, CIPAC 1, p. 965 may be useful.

1/ Should national pesticide specifications developed from these approved FAO specifications deviate from them, the national Authority responsible for making such changes is requested to inform the FAO Plant Protection Service of the nature of and the reasons for the modifications.

2/ Methods or analysis and miscellaneous techniques referred to in these specifications have been developed and adopted by CIPAC (Collaborative International Pesticides Analytical Council Ltd.). See CIPAC Handbooks, 1 (1970), 1A (1980), 1B (1983), 1C (1985) and ID (1988), CIPAC Proceedings 1980 and 1981, obtainable from Black Bear Press Limited, King's Hedges Road, Cambridge CB4 2PQ, England. The page numbers of specific methods are given in brackets in the specifications. A copy of a method not yet published can be obtained from the FAO Plant Protection Service.

3/ Information on standard waters for laboratory evaluation of pesticidal formulations will be found in "CIPAC Monograph 1, Standard Waters and an FAO survey on Naturally Occurring Waters" (1972). Black Bear Press Limited, King's Hedges Road, Cambridge CB4 2PQ, England.

SUBMISSION OF DRAFT SPECIFICATIONS TO FAO

Any organization, commercial firm or interested individual is encouraged to submit relevant specifications, or proposals for revision of existing specifications, for pesticide products for consideration and possible adoption by FAO. Correspondence should be addressed to the Pesticides Control Officer, Plant Production and Protection Division, FAO, Via delle Terme di Caracalla, 00100, Rome, Italy.

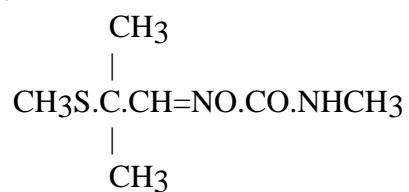
FAO has published a Manual on the development and use of FAO and WHO Specifications for Plant Protection Products, FAO Plant Production and Protection Paper No. 173, Rome 2002 (Revised First Edition available only on the FAO home page of the Internet at: <http://www.fao.org/pest-and-pesticide-management/en/>)

Specifications which are considered suitable for further processing are assigned priorities and circulated to appropriate organizations and specialists to comment. Comments, together with other relevant information, are then reviewed in detail by the Group on Specifications of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent. The drafts are converted into FAO Provisional Specifications, or full FAO Specifications.

INFORMATION

COMMON NAME: Aldicarb (ISO)

STRUCTURAL FORMULA:



EMPIRICAL FORMULA: $\text{C}_7\text{H}_{14}\text{N}_2\text{O}_2\text{S}$

RMM: 190.3

CAS REGISTRY NUMBER: 116-06-3

CIPAC CODE NUMBER: 215

CHEMICAL NAMES:

2-methyl-2-(methylthio)propionaldehyde 0-methylcarbamoxyloxime (IUPAC)

2-methyl-2-(methylthio)propanal 0[(methylamino)carbonyl]oxime (CA)

ALDICARB TECHNICAL
FAO Provisional Specification 215/TC/(S)/(1988)

.1 DESCRIPTION

The material shall consist of aldicarb together with related manufacturing impurities. It shall be white crystals free from visible extraneous matter and added modifying agents.

.2 ACTIVE INGREDIENT

.2.1 Identity Tests*

Where the identity of the material is in doubt, then it shall comply with at least one additional test.

.2.2 Aldicarb (215/1/M/1.3, CIPAC, 1A, p. 1094, CIPAC H, p. 10 (IR))

The aldicarb content shall be declared (minimum declared 920 g/kg) and when determined, the content obtained shall not differ from that declared by more than +/-20 g.

.3 IMPURITIES

.3.1 Manufacturing Impurities^{2*}

.3.1.1 Aldicarb Oxime	Maximum: 4.0 g/kg
.3.1.2 Methyl Isocyanate	Maximum: 12.5 g/kg
.3.1.3 Trimethylamine	Maximum: 12.5 g/kg
.3.1.4 Aldicarb Nitrile	Maximum: 35.0 g/kg
.3.1.5 Dimethylurea + Trimethylbiuret	Maximum: 50.0 g/kg

.3.2 Water (MT 30.1, CIPAC 1, p. 897)

Maximum: 2.5 g/kg

.4 PHYSICAL PROPERTIES

.4.1 pH of 1% Aqueous suspension (MT 75.2, CIPAC 1A, p. 1590)

Minimum pH: 5

Maximum pH: 8

² Method are available from the Plant Protection Officer, FAO, or download here here [Aldicarb Oxime](#), [Methyl Isocyanate](#), [Trimethylamine](#), [Aldicarb Nitrile](#), [Dimethylurea and Trimethylbiuret](#)

ALDICARB TECHNICAL CONCENTRATE
FAO Provisional Specification (215/TK/(S)/ (1988))

.1 DESCRIPTION

The material shall consist of aldicarb together with related manufacturing impurities and shall be a solution free from visible extraneous matter and added modifying agents. The solution shall be water clear to light amber in color.

.2 ACTIVE INGREDIENT

.2.1 Identity Tests

Where the identity of the active ingredient is in doubt, then the isolated active ingredient shall comply with at least one additional test.

.2.2 Aldicarb (215/1/M/1.3, CIPAC. 1A, p. 1094, CIPAC H, p. 10 (IR))

The aldicarb content shall be declared (minimum declared 356 g/kg) and when determined, the content obtained shall not differ from that by more than +/- 18g.

.3 IMPURITIES

.3.1 Manufacturing Impurities

.3.1.1 Aldicarb Oxime	Maximum:	1.0 g/kg
.3.1.2 Methyl Isocyanate	Maximum:	5.0 g/kg
.3.1.3 Trimethylamine	Maximum:	5.0 g/kg
.3.1.4 Aldicarb Nitrile	Maximum:	15.0 g/kg
.3.1.5 Dimethylurea + Trimethylbiuret	Maximum:	20.0 g/kg

.3.2 Water (MT 30.1, CIPAC 1, p.897)

Maximum: 1.0 g/kg

ALDICARB GRANULES
(For Application by Mechanical Equipment)
FAO Provisional Specification (215/GR/(S)/1988)

.1 DESCRIPTION

The material shall consist of granules containing technical or technical concentrate aldicarb [complying with the requirements of FAO Specifications 215/TC/(S)/(1988) or 215/TK/(S)/(1988), together with suitable carriers and any necessary formulants. It shall be dry, free from visible extraneous matter and hard lumps, free flowing, essentially non-dusty and intended for application by mechanical equipment.

.2 ACTIVE INGREDIENT

.2.1 Identity Tests

Where the identity of the active ingredient is in doubt, then the isolated active ingredient shall comply with at least one additional test.

.2.2 Aldicarb (215/12/M/1.3, CIPAC 1A, p.1095, CIPAC H, p. 10 (IR))

The aldicarb content shall be declared (g/kg) and when determined, the content obtained shall not differ from that declared by more than the following amounts:

<u>Declared Content</u>	<u>Permitted Tolerance</u>
up to 25 g/kg	+/- 20% of the declared content
above 25 g/kg up to 50 g/kg	+/- 15% of the declared content
above 50 g/kg up to 100 g/kg	+/- 10% of the declared content
above 100 g/kg	+/- 6% of the declared content

.3 PHYSICAL PROPERTIES

.3.1 Apparent density range after compaction without pressure (MT 58.4, CIPAC 1, p. 977)

The apparent density range after compaction without pressure shall be declared.

.3.2 Nominal size range (MT 58.3, CIPAC 1, p. 974)

The nominal size range of the product shall be declared (Note 1). The ratio of the lower to the upper declared limit shall not exceed 1:6 (Note 2). Not less than 85% of the product shall be within the declared nominal size range.

.3.3 Material retained on a 250 µm test sieve (MT 58.3, CIPAC 1, p. 974)

.4 STORAGE STABILITY

.4.1 Stability at 54°C

After storage at 54 +/- 2°C for 14 days, the product shall continue to comply with .2.2 (except that the minimum permitted aldicarb content shall be 95% of that found under .2.2), .3.2 and .3.3.

Note 1 e.g. 250 to 350 µm, 250 to 850 µm, 250 to 1410 µm, etc.

Note 2 Higher ratios may increase the risk of segregation which may adversely affect the flow rate. This should be checked with the machines to be used.

Bayer CropScience



STUDY TITLE

HPLC Determination of Methylisocyanate in Aldisol

(ALDICARB TECHNICAL SOLUTION)

Data Requirement

OECD Guidelines for Testing of Chemicals, Section 1 – Physical-Chemical Properties
EC Guidelines Part A – Methods for the Determination of Physico-Chemical Properties
EPA OPPTS Harmonized Test Guidelines Series 830 Product Properties Test
Guidelines

AUTHOR

Dr. Sarah Leibowitz

STUDY COMPLETION DATE

2004-02-26

PERFORMING LABORATORY

Bayer CropScience
NAFTA Analytical Services
8400 Hawthorn Road
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Submitting Laboratory Study Number

03S003

Bayer Report No.

G200970



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Quality Assurance Statement

Not applicable.


Approvals Page

Study director:
Bayer CropScience


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March 1, 2004
Date

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Bayer CropScience:


S. C. Slahck

March 1, 2004
Date

Submitter:
Bayer CropScience


S. C. Slahck

March 1, 2004
Date

Confidentiality Statement

This report is confidential. No part of the report or any information contained therein may be disclosed to any third party without the prior written authorization of Bayer CropScience.

HPLC Determination of Methylisocyanate in Aldisol™

Scope

This method is applicable to the determination of methylisocyanate in Aldisol (aldicarb technical solution).

Principle

Methylisocyanate is derivatized using dibutylamine as a derivatizing agent. Methylisocyanate content is determined by comparing the peak areas for the derivatized sample with corresponding derivatized standard of known percentage.

Reagents

<i>Reagent</i>	<i>Requirement</i>
Acetonitrile	HPLC grade
Dibutylamine	Acros Cat. #21982
Methylisocyanate	Analytical standard of known purity (P)
Methanol	HPLC grade
Methanol:water, 60:40	Mobile Solvent : Prepare by adding 600 mL of methanol to a bottle or flask containing 400 mL of deionized water. Mix the contents well. Add a few glass beads and degas the solvent mixture under a vacuum source while sonicating.
Water	Deionized

Equipment

<i>Equipment</i>	<i>Requirements</i>
Bath	Ultrasonic
HPLC Column	250 x 4.6-mm ID Zorbax, SB-C ₈ (5- μ m). Zorbax part # 880975 or equivalent.
Laboratory Data System	Waters Empower or equivalent
Liquid Chromatograph	Hewlett-Packard Model 1050 equipped with a variable wavelength detector, autoinjector, or equivalent equipment
Needle	Becton Dickinson Gauge 23G1
Syringe	1-mL, glass

Procedure

Danger: Aldicarb is an extremely toxic material. Proper PPE must be worn when handling samples. All sample preparation must be performed in a fume hood.

Aldisol is a trademark of Bayer CropScience

1. Set the following conditions on the instrument (different instruments may require slightly different conditions):

Parameter	Value	Units
Detector range ¹	1.0	V
Flow ²	1.2	mL/minute
Detector response ¹	1	sec
Injection volume	20	μL
Stop time	15	minutes
Range	2.0	AUFS
Wavelength	216	nm

¹Set these parameters using Control 11 and Control 7, respectively.

²Adjust the flow and solvent program as necessary to obtain resolution as shown in Figure 1.

2. Before injecting, pump mobile solvent through the column until the baseline becomes stable.
3. Add ca. 5 mL of acetonitrile to a 10-mL volumetric flask labeled "standard."
4. Using a 100-μL glass syringe, measure ca. 90 – 100 μL of methylisocyanate standard. Tare the balance. Transfer the entire syringe contents to the 10-mL volumetric flask from Step 3. Return the empty syringe to the balance. Record the weight ± 0.0001 g (W_s) of standard.
5. Dilute the contents to volume using acetonitrile. Mix the contents of the flask thoroughly.
6. Pipet 1.0 mL of standard solution into a 50-mL volumetric flask containing approximately 30 mL of acetonitrile. Add 50-μL of dibutylamine derivatizing agent.
7. Dilute the contents to volume using deionized water. Mix the contents thoroughly.
8. Similarly, add ca. 30 mL of acetonitrile to a 50-mL volumetric flask for the sample.
9. Using a glass syringe attached to a needle, measure ca. 0.9 - 1.0 mL of sample. Tare the balance. Transfer the entire syringe contents to the volumetric flask from Step 8. Return the empty syringe to the balance. Record the weight ± 0.0001 g (W) of sample.
10. Add 50 μL of dibutylamine to each volumetric flask from Step 9. Dilute the contents to volume using deionized water. Mix thoroughly.
11. Inject the standard solution from Step 7 in duplicate. Record the peak area of derivatized methylisocyanate as S. Compare methylisocyanate peak areas for the two injections. The areas must agree within 5.0% ($\pm 2.5\%$ of their average), otherwise, reinject the standard solution until 2 successive injections do agree. Figure 1 shows a typical standard chromatogram and Figure 3 list typical computer parameters.
12. Inject the sample solution from Step 10 once. Record the peak area for methylisocyanate as A. Figure 2 shows a typical sample chromatogram.

13. Inject the standard solution again after every 2 – 3 samples and again at the end of the run. Bracketing standards must meet the agreement criterion in Step 11.

Calculations

$$\text{Methylisocyanate \%} = \frac{W_s \times P \times A}{W \times S}$$

Symbol	Description
W_s	Standard weight, grams
W	Sample weight, grams
P	Purity percentage of component n in the standard
I	Peak area of the internal standard for the standard chromatogram
S	Peak area of component n in the standard chromatogram
A	Peak area of component n in the sample chromatogram
B	Peak area of the internal standard for the sample chromatogram

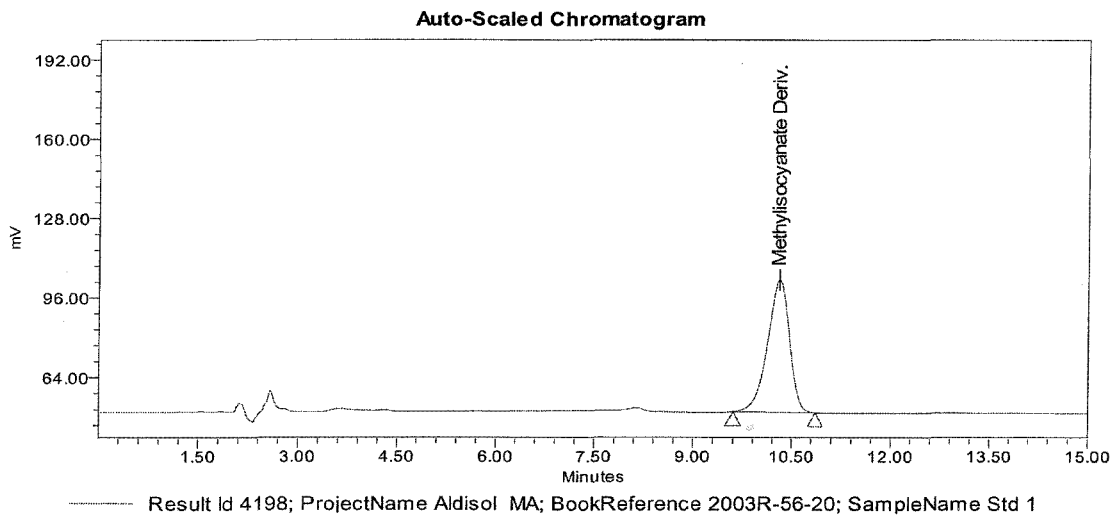


Figure 1. Typical Standard Chromatogram.

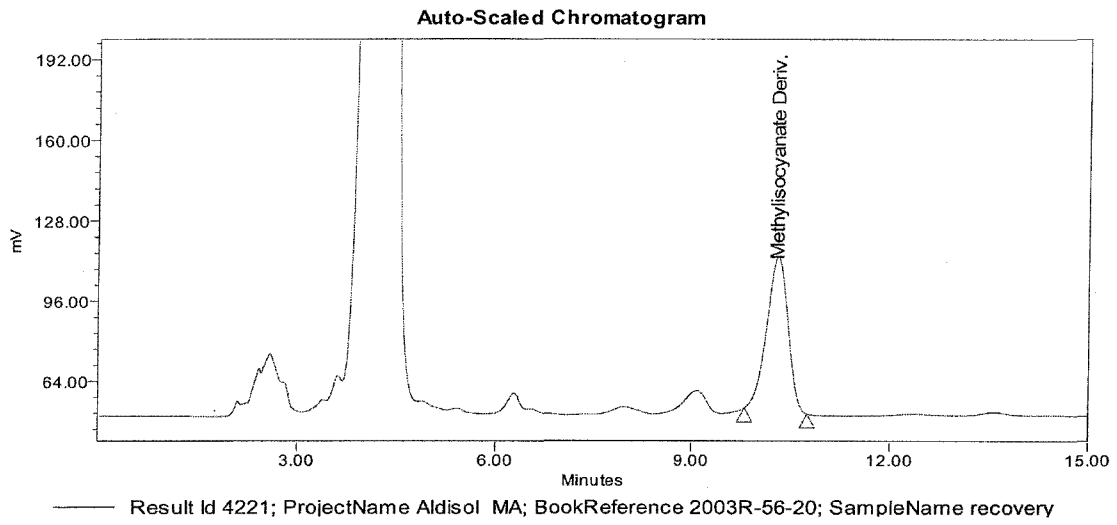


Figure 2. Typical Sample Chromatogram.

Processing Parameters**Integration Parameters**

<i>Parameter</i>	<i>Units</i>	<i>Value</i>
Minimum Area	$\mu\text{V}\cdot\text{sec}$	10000
Minimum Height	μV	3800
Threshold	$\mu\text{V}\cdot\text{sec}$	100
Width	sec	30

Components

<i>Field</i>	<i>Value</i>
RT Window %	10
Update RT	Never

<i>Name</i>	<i>Retention Time, minutes</i>	<i>Retention Time Window</i>	<i>Y Value</i>	<i>Internal Standard</i>	<i>Default Units</i>	<i>CcompRefI</i>
Methylisocyanate Derivative	10.0	0.9	Area		%	

Default Amounts

<i>Level</i>	<i>Methylisocyanate Derivative</i>
Purity	98.0
Combo Factor	1
Multiple Standard Weights	1

Figure 3. Typical Computer Parameters.

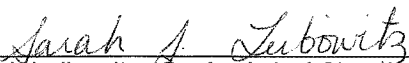
Validation data

This method was validated using batches of Aldisol (aldicarb technical solution) and methylisocyanate Analytical standard.

Precision:	Methylisocyanate: CV=0.05% (CV = relative standard deviation, obtained by threefold analysis)
Linearity range:	Methylisocyanate: 20 – 200% (w/w) (of the nominal methylisocyanate concentration)
Working range:	Methylisocyanate: 0.037 - 0.37 mg/mL (of methylisocyanate in solution)
Accuracy:	Methylisocyanate: 81.7% (based on the analysis of a standard addition to Aldisol sample)
Limit of detection:	Methylisocyanate 0.002%
Limit of quantification:	Methylisocyanate 0.004%
Specificity:	The specificity is demonstrated by no interference from reagent blanks.
Stability:	The reference solution and sample solution are stable at least for 12 hours at ambient temperature.

Approvals

Written By:


S. J. Leibowitz - Sr. Analytical Chemist

Approved By:


S.C. Slahck - Manager, NAFTA Analytical Services**Cross-References**

Reference	Reference Title
TM A-54.11	General Procedure for Waters Empower Laboratory Automation System
CM-88	Aventis – Methylisocyanate Analysis in Aldicarb Solution or Recovered Methylisocyanate by Liquid Chromatography; 5-3-1993.
LC03	Fee Code

Bayer CropScience



STUDY TITLE

HPLC Determination of Aldicarb Impurities

Data Requirement

OECD Guidelines for Testing of Chemicals, Section 1 – Physical-Chemical Properties
EC Guidelines Part A – Methods for the Determination of Physico-Chemical Properties
EPA OPPTS Harmonized Test Guidelines Series 830 Product Properties Test
Guidelines

AUTHOR

Dr. Sarah Leibowitz

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2004-02-26

PERFORMING LABORATORY

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SUBMITTING LABORATORY STUDY NUMBER

03S003

BAYER REPORT NO.

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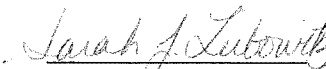
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Not applicable.


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Submitter:
Bayer CropScience


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March 1, 2004
Date

Confidentiality Statement

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HPLC Determination of Aldicarb Impurities

Scope

This method is applicable to the determination of Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret in Aldisol™ (aldicarb technical solution).

Principle

Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret are determined by comparing the peak areas for the sample with corresponding standards of known percentage purity using acetanilide as an internal standard.

Reagents

<i>Reagent</i>	<i>Requirements</i>
Aldicarb nitrile	Analytical standard of known percentage purity (P ₁)
Aldicarb oxime	Analytical standard of known percentage purity (P ₂)
Acetanilide	Acros # AC15081-2500 or equivalent
Acetanilide, 0.003% (v/v) in methanol	Internal Standard Solution: Prepare by weighing 0.03 g of acetanilide into a bottle containing 1 L of methanol.
1,3-Dimethylurea	Analytical standard of known percentage purity (P ₃)
Methanol:water, 15:85	Mobile Solvent A: Prepare by adding 150 mL of methanol to a bottle or flask containing 850 mL of deionized water. Mix the contents well. Add a few glass beads and degas the solvent mixture under a vacuum source while sonicating.
Methanol:water, 30:70	Mobile Solvent B: Prepare by adding 300 mL of methanol to a bottle or flask containing 700 mL of deionized water. Mix the contents well. Add a few glass beads and degas the solvent mixture under a vacuum source while sonicating.
1,3,5-Trimethylbiuret	Analytical standard of known percentage purity (P ₄)
Water	Deionized

Aldisol is a trademark of Bayer CropScience

Equipment

<i>Equipment</i>	<i>Requirements</i>
Bath	Ultrasonic
HPLC Column	250 x 4.6-mm ID Zorbax Rx-C ₈ (5- μ m). Zorbax part # 880967 or equivalent.
Laboratory Data System	Waters Empower or equivalent
Liquid Chromatograph	Hewlett-Packard Model 1050 equipped with a variable wavelength detector, autoinjector, or equivalent equipment
Needle	Becton Dickinson Gauge 23G1
Syringe	1-mL, glass

Procedure

Danger: Aldicarb is an extremely toxic material. Proper PPE must be worn when handling samples. All sample preparation must be performed in a fume hood.

1. Set the following conditions on the instrument (different instruments may require slightly different conditions):

<i>Parameter</i>	<i>Value</i>	<i>Units</i>
Detector range ¹	1.0	V
Flow ²	1.7	mL/minute
Detector response ¹	1	sec
Injection volume	10	μ L
Stop time	30	minutes
Range	2.0	AUFS
Wavelength	205	nm
Solvents		
	A	Mobile Phase A
	B	Mobile Phase B
Solvent Program		
	Time, Minutes	%B
	Initial	0
	7.5	0
	8.5	100
	26.0	100
	27.0	0

¹Set these parameters using Control 11 and Control 7, respectively.

²Adjust the flow and solvent program as necessary to obtain resolution as shown in Figure 1.

2. Before injecting, pump mobile solvent through the column until the baseline becomes stable.
3. To prepare the impurities standard solution, weigh 0.014 – 0.016 \pm 0.0001 g (W_1) of Aldicarb Nitrile, 0.0008 – 0.0015 g \pm 0.0001 g (W_2) of Aldicarb Oxime, 0.004 – 0.008 \pm

0.0001 g (W_3) of 1,3-dimethylurea, and 0.004 – 0.008 g \pm 0.0001 g (W_4) of 1,3,5-trimethylbiuret analytical standards into a single 1/2-oz. bottle.

4. Pipet 10.0 mL of internal standard solution into the standard bottle from Step 3 and bottles to prepare all sample solutions in Step 5.
5. Using a glass syringe attached to a needle, measure ca. 0.5 - 0.7 mL of sample. Tare the balance. Transfer the entire syringe contents to the 1/2-oz. sample bottle. Return the empty syringe to the balance. Record the weight \pm 0.0001 g (W) of sample.
6. Cap and shake the bottles from Steps 4 and 5 vigorously to mix.
7. Inject the standard solution from Step 6 in duplicate. Record the peak areas of the acetanilide, Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret peaks as I, S_1 , S_2 , S_3 , and S_4 , respectively. Compare the internal standard:component peak area ratios, R_n , for each injection. The ratios must agree within 5.0% ($\pm 2.5\%$ of their average), otherwise, reinject the standard solution until 2 successive injections do agree. Figure 1 shows a typical standard chromatogram and Figure 3 lists typical computer parameters.
8. Inject each sample solution from Step 6 once. Record the peak areas for acetanilide, Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret as B and A_1 , A_2 , A_3 , and A_4 respectively. A typical sample chromatogram is shown in Figure 2.
9. Inject the standard solution again after every 5 – 6 samples and again at the end of the run. Bracketing standards must meet the agreement criterion in Step 7.

Calculations:

$$R_n = \frac{I}{S_n} \quad M = \frac{A_n}{B} \quad K_n = W_{S_n} \times P_n \times \bar{R}_n$$

$$\text{Analyte } n, \% = \frac{K_n \times M_n}{W}$$

Symbol	Description
A	Peak area of component n in the sample chromatogram
B	Peak area of the internal standard for the sample chromatogram
I	Peak area of the internal standard for the standard chromatogram
P	Purity percentage of component n in the standard
S	Peak area of component n in the standard chromatogram
W	Sample weight, grams
W_s	Standard weight, grams

- Where n =
- 1 For Aldicarb Nitrile
 - 2 For Aldicarb Oxime
 - 3 For 1,3-dimethylurea
 - 4 For 1,3,5-trimethylbiuret

Chromatograms:

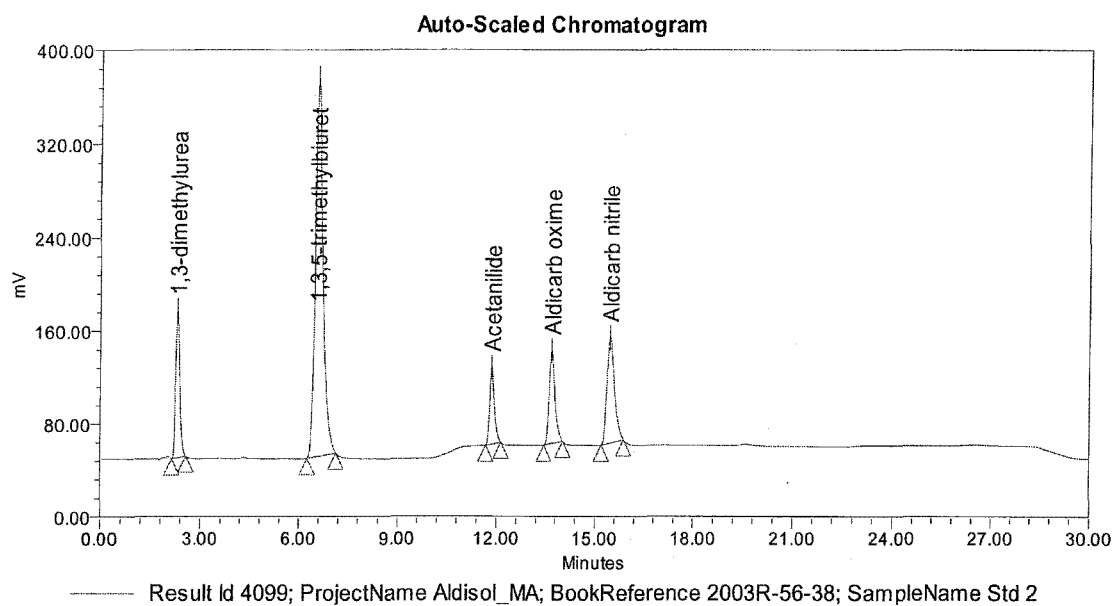


Figure 1. Typical Standard Chromatogram.

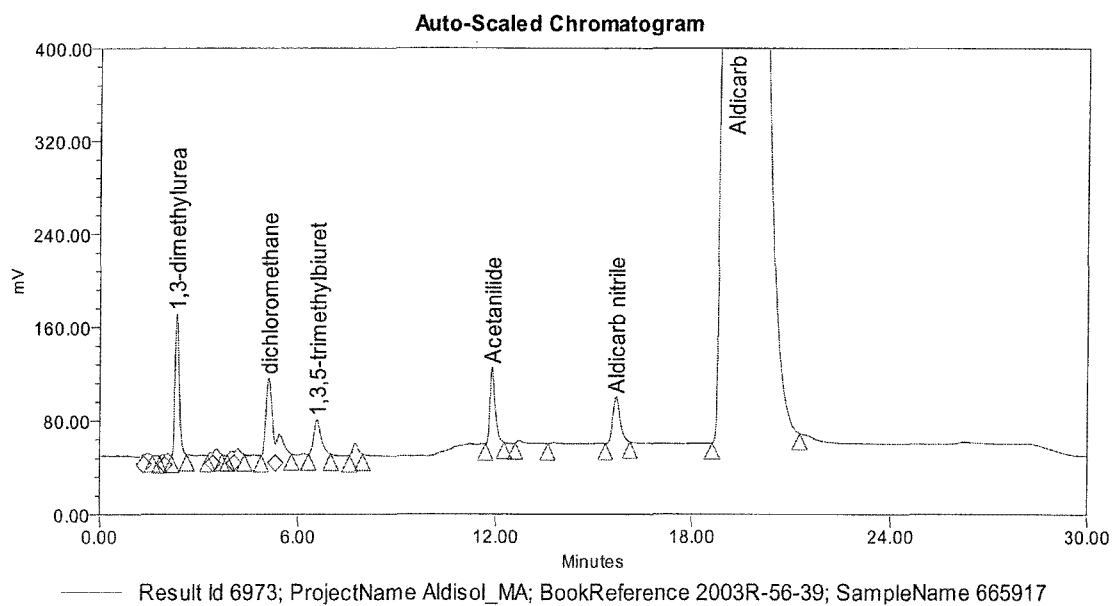


Figure 2. Typical Sample Chromatogram

Processing Parameters**Integration Parameters**

<i>Parameter</i>	<i>Units</i>	<i>Value</i>
Minimum Area	$\mu\text{V} \cdot \text{sec}$	5000
Minimum Height	μV	100
Threshold	$\mu\text{V} \cdot \text{sec}$	100
Width	sec	20

Components

<i>Field</i>	<i>Value</i>
RT Window %	5
Update RT	Never

<i>Name</i>	<i>Retention Time, minutes</i>	<i>Retention Time Window</i>	<i>Y Value</i>	<i>Internal Standard</i>	<i>Default Units</i>	<i>CcompRef1</i>
1,3-dimethylurea	2.3	0.125	Area	Acetanilide	%	
1,3,5-Trimethylbiuret	6.6	0.330	Area	Acetanilide	%	
Acetanilide	11.8	.590	Area			
Aldicarb Oxime	13.6	.770	Area	Acetanilide	%	
Aldicarb Nitrile	15.3	.850	Area	Acetanilide	%	
Aldicarb	21.0	.950	Area			

Default Amounts

<i>Level</i>	<i>1,3-Dimethylurea</i>	<i>1,3,5-trimethylbiuret</i>	<i>Acetanilide</i>	<i>Aldicarb Oxime</i>	<i>Aldicarb Nitrile</i>
Purity	99.2	99.7	100	99.1	99.0
Combo Factor	1	1	1	1	1
Multiple Standard Weights	1	1	1	1	1

Figure 3. Typical Computer Parameters.

Validation data

This method was validated using batches of Aldisol (aldicarb technical solution) and aldicarb nitrile, aldicarb oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret Analytical standards.

Precision:	Aldicarb Nitrile: CV=0.02% Aldicarb Oxime: CV= N/A 1,3-Dimethylurea: CV = 0.02% 1,3,5-Trimethylbiuret: CV = 0.03% (CV = relative standard deviation, obtained by threefold analysis)
Linearity range:	Aldicarb Nitrile: 20 – 200% (w/w) Aldicarb Oxime: 20 – 200% (w/w) 1,3-Dimethylurea: 20 – 200% (w/w) 1,3,5-Trimethylbiuret: 20 – 200% (w/w) (of the nominal Analyte concentration) Acetanilide (internal standard): 20 – 200% (w/w) (of the nominal acetanilide concentration)
Working range:	Aldicarb Nitrile: 0.29 - 2.9 mg/mL Aldicarb Oxime: 0.07 - 0.7 mg/mL 1,3-Dimethylurea: 0.12 - 1.2 mg/mL 1,3,5-Trimethylbiuret: 0.14 - 1.4 mg/mL (of the component in solution) Acetanilide: 0.87 – 8.7 mg/100 mL (of the component in solution)
Accuracy:	Aldicarb Nitrile : 113% Aldicarb Oxime: N/A 1,3-Dimethylurea: 97.7% 1,3,5-trimethylurea: 117% (based on the analysis of a standard addition to Aldisol sample)
Limit of detection:	Aldicarb Nitrile 0.02% Aldicarb Oxime 0.02% 1,3-Dimethylurea 0.01% 1,3,5-Trimethylbiuret 0.01%
Limit of quantification:	Aldicarb Nitrile 0.04% Aldicarb Oxime 0.04% 1,3-Dimethylurea 0.02% 1,3,5-Trimethylbiuret 0.02%
Specificity:	The specificity is demonstrated by no interference from reagent blanks or internal standard. Sufficient separation of impurities and the internal standard are demonstrated in the chromatogram, Figure 2.
Stability:	The reference solution and sample solution are stable for at least 24 hours at ambient temperature.

Approvals

Written By:

Sarah J. Leibowitz
S. J. Leibowitz - Sr. Analytical Chemist

Approved By:

Stephen C. Slahck
S.C. Slahck - Manager, NAFTA Analytical Services

Cross-References

Reference	Reference Title
TM A-54.11	General Procedure for Waters Empower Laboratory Automation System
CM-9052	Aventis - Aldicarb Purity by HPLC; 6-1-2003
LC04	Fee Code

Bayer CropScience



STUDY TITLE

HPLC Determination of Aldicarb Impurities

Data Requirement

OECD Guidelines for Testing of Chemicals, Section 1 – Physical-Chemical Properties
EC Guidelines Part A – Methods for the Determination of Physico-Chemical Properties
EPA OPPTS Harmonized Test Guidelines Series 830 Product Properties Test
Guidelines

AUTHOR

Dr. Sarah Leibowitz

STUDY COMPLETION DATE

2004-02-26

PERFORMING LABORATORY

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SUBMITTING LABORATORY STUDY NUMBER

03S003

BAYER REPORT NO.

G200968



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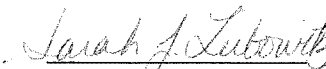
This page is intentionally left blank for the purpose of submitting administrative information that is required by regulations promulgated by various countries.

Quality Assurance Statement

Not applicable.


Approvals Page

Study director:
Bayer CropScience


Dr. S. J. Leibowitz


March 1, 2004
Date

Sponsor:
Bayer CropScience:


S. C. Slahck

March 1, 2004
Date

Submitter:
Bayer CropScience


S. C. Slahck

March 1, 2004
Date

Confidentiality Statement

This report is confidential. No part of the report or any information contained therein may be disclosed to any third party without the prior written authorization of Bayer CropScience.

HPLC Determination of Aldicarb Impurities

Scope

This method is applicable to the determination of Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret in Aldisol™ (aldicarb technical solution).

Principle

Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret are determined by comparing the peak areas for the sample with corresponding standards of known percentage purity using acetanilide as an internal standard.

Reagents

<i>Reagent</i>	<i>Requirements</i>
Aldicarb nitrile	Analytical standard of known percentage purity (P ₁)
Aldicarb oxime	Analytical standard of known percentage purity (P ₂)
Acetanilide	Acros # AC15081-2500 or equivalent
Acetanilide, 0.003% (v/v) in methanol	Internal Standard Solution: Prepare by weighing 0.03 g of acetanilide into a bottle containing 1 L of methanol.
1,3-Dimethylurea	Analytical standard of known percentage purity (P ₃)
Methanol:water, 15:85	Mobile Solvent A: Prepare by adding 150 mL of methanol to a bottle or flask containing 850 mL of deionized water. Mix the contents well. Add a few glass beads and degas the solvent mixture under a vacuum source while sonicating.
Methanol:water, 30:70	Mobile Solvent B: Prepare by adding 300 mL of methanol to a bottle or flask containing 700 mL of deionized water. Mix the contents well. Add a few glass beads and degas the solvent mixture under a vacuum source while sonicating.
1,3,5-Trimethylbiuret	Analytical standard of known percentage purity (P ₄)
Water	Deionized

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Equipment

<i>Equipment</i>	<i>Requirements</i>
Bath	Ultrasonic
HPLC Column	250 x 4.6-mm ID Zorbax Rx-C ₈ (5- μ m). Zorbax part # 880967 or equivalent.
Laboratory Data System	Waters Empower or equivalent
Liquid Chromatograph	Hewlett-Packard Model 1050 equipped with a variable wavelength detector, autoinjector, or equivalent equipment
Needle	Becton Dickinson Gauge 23G1
Syringe	1-mL, glass

Procedure

Danger: Aldicarb is an extremely toxic material. Proper PPE must be worn when handling samples. All sample preparation must be performed in a fume hood.

1. Set the following conditions on the instrument (different instruments may require slightly different conditions):

<i>Parameter</i>	<i>Value</i>	<i>Units</i>
Detector range ¹	1.0	V
Flow ²	1.7	mL/minute
Detector response ¹	1	sec
Injection volume	10	μ L
Stop time	30	minutes
Range	2.0	AUFS
Wavelength	205	nm
Solvents		
A	Mobile Phase A	
B	Mobile Phase B	
Solvent Program		
	Time, Minutes	%B
	Initial	0
	7.5	0
	8.5	100
	26.0	100
	27.0	0

¹Set these parameters using Control 11 and Control 7, respectively.

²Adjust the flow and solvent program as necessary to obtain resolution as shown in Figure 1.

2. Before injecting, pump mobile solvent through the column until the baseline becomes stable.
3. To prepare the impurities standard solution, weigh 0.014 – 0.016 \pm 0.0001 g (W_1) of Aldicarb Nitrile, 0.0008 – 0.0015 g \pm 0.0001 g (W_2) of Aldicarb Oxime, 0.004 – 0.008 \pm

0.0001 g (W_3) of 1,3-dimethylurea, and 0.004 – 0.008 g \pm 0.0001 g (W_4) of 1,3,5-trimethylbiuret analytical standards into a single 1/2-oz. bottle.

4. Pipet 10.0 mL of internal standard solution into the standard bottle from Step 3 and bottles to prepare all sample solutions in Step 5.
5. Using a glass syringe attached to a needle, measure ca. 0.5 - 0.7 mL of sample. Tare the balance. Transfer the entire syringe contents to the 1/2-oz. sample bottle. Return the empty syringe to the balance. Record the weight \pm 0.0001 g (W) of sample.
6. Cap and shake the bottles from Steps 4 and 5 vigorously to mix.
7. Inject the standard solution from Step 6 in duplicate. Record the peak areas of the acetanilide, Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret peaks as I, S_1 , S_2 , S_3 , and S_4 , respectively. Compare the internal standard:component peak area ratios, R_n , for each injection. The ratios must agree within 5.0% ($\pm 2.5\%$ of their average), otherwise, reinject the standard solution until 2 successive injections do agree. Figure 1 shows a typical standard chromatogram and Figure 3 lists typical computer parameters.
8. Inject each sample solution from Step 6 once. Record the peak areas for acetanilide, Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret as B and A_1 , A_2 , A_3 , and A_4 respectively. A typical sample chromatogram is shown in Figure 2.
9. Inject the standard solution again after every 5 – 6 samples and again at the end of the run. Bracketing standards must meet the agreement criterion in Step 7.

Calculations:

$$R_n = \frac{I}{S_n} \quad M = \frac{A_n}{B} \quad K_n = W_{Sn} \times P_n \times \bar{R}_n$$

$$\text{Analyte } n, \% = \frac{K_n \times M_n}{W}$$

Symbol	Description
A	Peak area of component n in the sample chromatogram
B	Peak area of the internal standard for the sample chromatogram
I	Peak area of the internal standard for the standard chromatogram
P	Purity percentage of component n in the standard
S	Peak area of component n in the standard chromatogram
W	Sample weight, grams
W_s	Standard weight, grams

- Where n =
- 1 For Aldicarb Nitrile
 - 2 For Aldicarb Oxime
 - 3 For 1,3-dibutylurea
 - 4 For 1,3,5-trimethylbiuret

Chromatograms:

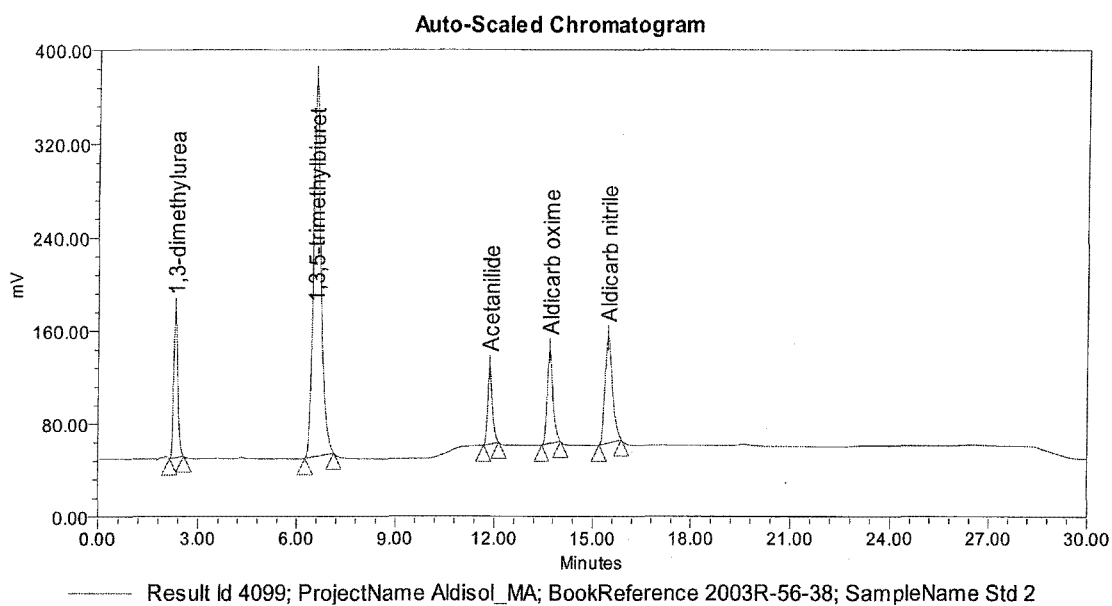


Figure 1. Typical Standard Chromatogram.

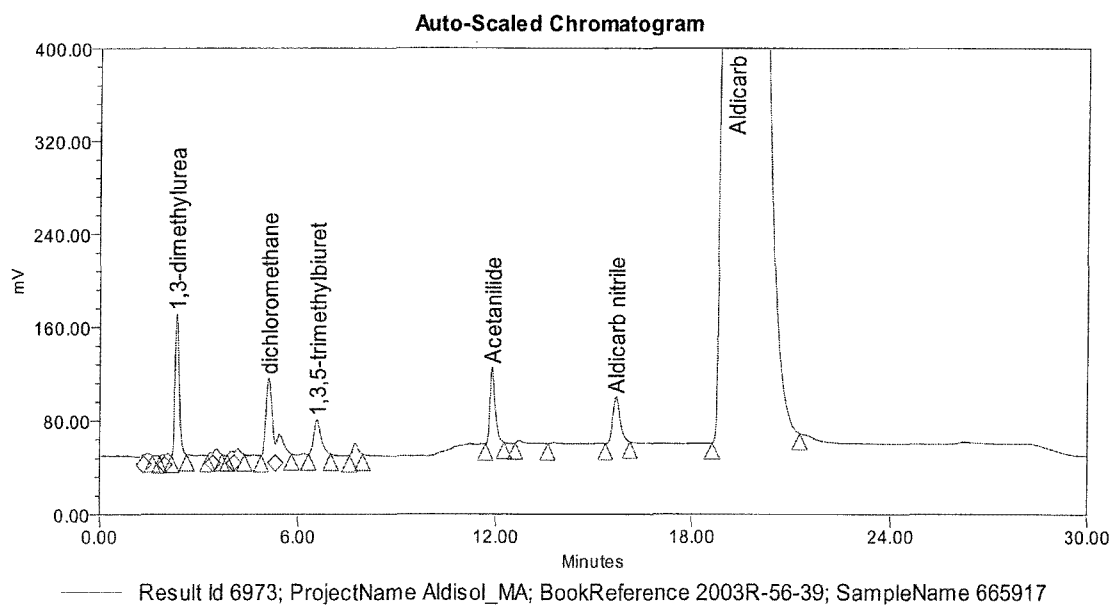


Figure 2. Typical Sample Chromatogram

Processing Parameters**Integration Parameters**

<i>Parameter</i>	<i>Units</i>	<i>Value</i>
Minimum Area	$\mu\text{V}*\text{sec}$	5000
Minimum Height	μV	100
Threshold	$\mu\text{V}*\text{sec}$	100
Width	sec	20

Components

<i>Field</i>	<i>Value</i>
RT Window %	5
Update RT	Never

<i>Name</i>	<i>Retention Time, minutes</i>	<i>Retention Time Window</i>	<i>Y Value</i>	<i>Internal Standard</i>	<i>Default Units</i>	<i>CcompRef1</i>
1,3-dimethylurea	2.3	0.125	Area	Acetanilide	%	
1,3,5-Trimethylbiuret	6.6	0.330	Area	Acetanilide	%	
Acetanilide	11.8	.590	Area			
Aldicarb Oxime	13.6	.770	Area	Acetanilide	%	
Aldicarb Nitrile	15.3	.850	Area	Acetanilide	%	
Aldicarb	21.0	.950	Area			

Default Amounts

<i>Level</i>	<i>1,3-Dimethylurea</i>	<i>1,3,5-trimethylbiuret</i>	<i>Acetanilide</i>	<i>Aldicarb Oxime</i>	<i>Aldicarb Nitrile</i>
Purity	99.2	99.7	100	99.1	99.0
Combo Factor	1	1	1	1	1
Multiple Standard Weights	1	1	1	1	1

Figure 3. Typical Computer Parameters.

Validation data

This method was validated using batches of Aldisol (aldicarb technical solution) and aldicarb nitrile, aldicarb oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret Analytical standards.

Precision:	Aldicarb Nitrile: CV=0.02% Aldicarb Oxime: CV= N/A 1,3-Dimethylurea: CV = 0.02% 1,3,5-Trimethylbiuret: CV = 0.03% (CV = relative standard deviation, obtained by threefold analysis)
Linearity range:	Aldicarb Nitrile: 20 – 200% (w/w) Aldicarb Oxime: 20 – 200% (w/w) 1,3-Dimethylurea: 20 – 200% (w/w) 1,3,5-Trimethylbiuret: 20 – 200% (w/w) (of the nominal Analyte concentration) Acetanilide (internal standard): 20 – 200% (w/w) (of the nominal acetanilide concentration)
Working range:	Aldicarb Nitrile: 0.29 - 2.9 mg/mL Aldicarb Oxime: 0.07 - 0.7 mg/mL 1,3-Dimethylurea: 0.12 - 1.2 mg/mL 1,3,5-Trimethylbiuret: 0.14 - 1.4 mg/mL (of the component in solution) Acetanilide: 0.87 – 8.7 mg/100 mL (of the component in solution)
Accuracy:	Aldicarb Nitrile : 113% Aldicarb Oxime: N/A 1,3-Dimethylurea: 97.7% 1,3,5-trimethylurea: 117% (based on the analysis of a standard addition to Aldisol sample)
Limit of detection:	Aldicarb Nitrile 0.02% Aldicarb Oxime 0.02% 1,3-Dimethylurea 0.01% 1,3,5-Trimethylbiuret 0.01%
Limit of quantification:	Aldicarb Nitrile 0.04% Aldicarb Oxime 0.04% 1,3-Dimethylurea 0.02% 1,3,5-Trimethylbiuret 0.02%
Specificity:	The specificity is demonstrated by no interference from reagent blanks or internal standard. Sufficient separation of impurities and the internal standard are demonstrated in the chromatogram, Figure 2.
Stability:	The reference solution and sample solution are stable for at least 24 hours at ambient temperature.

Approvals

Written By:

Sarah J. Leibowitz
S. J. Leibowitz - Sr. Analytical Chemist

Approved By:

Stephen C. Slahck
S.C. Slahck - Manager, NAFTA Analytical Services

Cross-References

Reference	Reference Title
TM A-54.11	General Procedure for Waters Empower Laboratory Automation System
CM-9052	Aventis - Aldicarb Purity by HPLC; 6-1-2003
LC04	Fee Code

Bayer CropScience



STUDY TITLE

Determination of Trimethylamine (TMA) in Aldisol by Titration

(ALDICARB TECHNICAL SOLUTION)

Data Requirement

OECD Guidelines for Testing of Chemicals, Section 1 – Physical-Chemical Properties
EC Guidelines Part A – Methods for the Determination of Physico-Chemical Properties
EPA OPPTS Harmonized Test Guidelines Series 830 Product Properties Test
Guidelines

AUTHOR

Dr. Sarah Leibowitz

STUDY COMPLETION DATE

2004-02-26

PERFORMING LABORATORY

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SUBMITTING LABORATORY STUDY NUMBER

03S003

BAYER REPORT NO.

G200972



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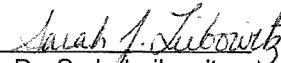
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Quality Assurance Statement

Not applicable.

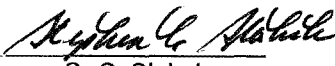
Approvals Page

Study director:
Bayer CropScience


Dr. S. J. Leibowitz

March 1, 2004
Date

Sponsor:
Bayer CropScience:


S. C. Slahck

March 1, 2004
Date

Submittor:
Bayer CropScience


S. C. Slahck

March 1, 2004
Date

Confidentiality Statement

This report is confidential. No part of the report or any information contained therein may be disclosed to any third party without the prior written authorization of Bayer CropScience.

Determination of Trimethylamine (TMA) by Titration

Scope

This method is applicable to trimethylamine in Aldisol.TM

Principle

TMA content in Aldisol is titrated with hydrochloric acid of known normality.

Reagents

<i>Reagent</i>	<i>Requirement</i>
Acetone	ACS grade
Buffer solutions, pH 7 and pH 4	Certified
Electrode storage solution.	3M Potassium chloride (KCl). Dissolve 22.4 g of KCl into 100 mL of deionized water.
Hydrochloric acid, HCl	Certified ACS plus, Fisher Cat. No. A144
Hydrochloric acid, 1.0N in isopropyl alcohol	Prepared by adding approximately 10 mL of concentrated HCl to a 100-mL volumetric flask. Dilute the contents to volume using isopropyl alcohol. Mix the contents thoroughly.
Hydrochloric acid, 0.02N in isopropyl alcohol	Pipet 5.0 mL of 1.0N hydrochloric acid solution into a 250 mL volumetric flask. Dilute the contents to volume using isopropyl alcohol. Mix the contents thoroughly.
Isopropyl alcohol	Fisher Cat. No. A459
Methanol	ACS grade, Fisher Cat. No. A454-1
Phenolphthalein	ACS grade, Fisher Cat. No. P79
Phenolphthalein, 1%	Prepare by weighing 1.0 g of phenolphthalein into a 100-mL volumetric flask. Dilute the contents to volume with methanol. Mix the solution thoroughly.
Sodium hydroxide, 0.1N	Purchased from Fisher, Cat. No. 12426
Sodium hydroxide, 0.01N	Prepare by pipetting 20.0 mL of 0.1N sodium hydroxide solution into a 200-mL volumetric flask. Dilute the contents to volume using deionized water. Mix the solution thoroughly.
Water	Deionized

Equipment

<i>Equipment</i>	<i>Requirement</i>
Autotitrator	Metrohm Model 751 GPD Titrino, equipped with a keyboard, a Model 728 stirrer, a Model 6.0220.100 combination pH glass electrode, and a Seiko DPU-411 Type II thermal printer, or equivalent equipment.
Needle	Becton Dickinson Gauge 23G1
Stirring bar	1-inch

Aldisol is a trademark of Bayer CropScience

Procedure

Danger: Aldicarb is an extremely toxic material. Proper PPE must be worn when handling samples. All sample preparation and titrations must be performed in a fume hood.

1. To standardize the 0.02N HCl solution, titrate with 0.01N sodium hydroxide (NaOH) as follows.
2. Using a buret, add 16 mL and 17 mL of 0.02N HCl solution to separate 250-mL Erlenmeyer flasks.
3. Add 4 - 5 drops of 1% phenolphthalein solution to each as an indicator.
4. Titrate the 2 solutions from Step 3 with 0.01N NaOH to the first pink color that lasts for 15 seconds.
5. Calculate the exact normality, N_2 , of the 0.02N hydrochloric acid solution. The 2 values must agree within 1% ($\pm 0.05\%$ of their average), otherwise repeat Steps 2 -5.
6. To determine the amount of trimethylamine in the sample, place 50 mL of isopropyl alcohol and 10 mL of deionized water into a 250-mL beaker.
7. Using a 5-mL glass syringe attached to a needle, measure ca. 5 mL of the sample. Place the syringe on a balance. Tare the balance.
8. Transfer the contents of the syringe to the beaker from Step 6.
9. Put the empty syringe back on the balance. Record the sample weight $\pm 0.0001\text{g}$.
10. Turn on the titrator and the printer.
11. Remove air from the buret and titrant line by submerging the titrant line's tip under water in a waste beaker. The tip has a resistor that will cause the titrant to splatter unless submerged in liquid. Press **PREP** (the "4" key) repeatedly until "internal DØ prep" appears on the display screen. Press **START** when finished. Rinse the tip with deionized water.
12. Calibrate the titrator using buffer solutions at pH 7.00 and 4.00. The calibration is acceptable for a 24-hour period.
13. Recall Method "B-100.5" from the internal memory of the titrator using the following steps (Typical titration parameters are shown in Figure 1):
 - a. Press **USER METH**, (the "3" key).
 - b. "Recall Method" will be highlighted. Press **ENTER**.
 - c. Using the ← or → key, scroll through the methods until "B-100.05" appears on the screen. Press **ENTER**. The display screen will show "DET pH DØaB-100.05".
 - d. If the wrong button is pushed, press **QUIT** to return to the previous screen.

14. Insert the pH electrode and titrant line tip into the sample beaker from Step 2.
15. Press **START** to start the stirrer and the titration. The titration can be stopped manually by pressing **STOP** at any time.
16. Enter the sample's LIMS number as the sample identity, or id1. Press **ENTER**.
17. Enter the sample weight in grams. Press **ENTER**.
18. Using the ← or → key, scroll through the units of measure until "g" appears. Press **ENTER**.
19. The titrator will pause for 60 seconds before recording the initial pH, shown as pHc(init) on the report. The display screen will show the titration curve on a pH vs. volume (mL) scale as the sample is titrated. If after the 60 second pause the pH of the solution is 7.0 or greater, the titrator will automatically stop and print the report.
20. The titration stops automatically after the endpoint, EP1, is detected, and the amount of TMA in the sample is calculated. The titrator will also automatically stop if it dispenses 50 mL of titrant.
21. The printout should be similar to Figure 2. Report the initial pH, shown as "pHc (init)" on the printout, and the calculated TMA as milliequivalents of TMA per gram (meq/g).
22. Rinse the pH electrode with deionized water and blot it with a tissue. Store it in the electrode storage solution, submerging the glass bulb.
23. Turn off the titrator and the printer.

Calculations

$$\text{Normality HCl, } N_2 = \frac{N_1 \times V_1}{V_2}$$

$$\text{TMA, \%} = \frac{V_3 \times N_2 \times 5.900}{W}$$

Symbol	Description
N ₁	Normality of NaOH
N ₂	Normality of HCl
V ₁	Volume of NaOH
V ₂	Volume of HCl required for the standardization
V ₃	Volume of 0.02N HCl required for determination of TMA
W	Sample weight

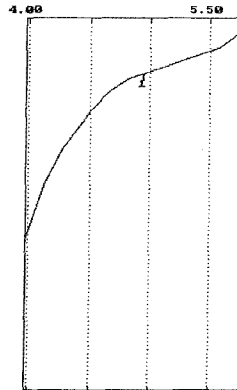
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>preselections
  req.ident:           id1
  req.smpl size:      all
  activate pulse:     OFF

```

Figure 1. Typical Titration Parameters

```
'cu
751 GPD Titrimo      04261      751.0010
date 03-12-16      time 16:03      2
start V      0.000 mL DET pH      B-100.05
5.0
dpH=1.0/div
```



=====

```
'fm
751 GPD Titrimo      04261      751.0010
date 03-12-16      time 16:03      2
DET pH      B-100.05
>calculations
ACIDITY=EP1*C39/C00*3;meq/g
C00=      5.0547 Sample amount
C39=      0.0200 HCl normality
```

```
'cr
751 GPD Titrimo      04261      751.0010
date 03-12-16      time 14:35      2
meas.input:      1      CAL
cal.date      03-12-16
pH      U/mV
buffer 1      7.00      -37
buffer 2      4.00      138
cal.temp      25.0 C
slope(rel)      1.000      pH(as)      7.00
```

```
'fr
751 GPD Titrimo      04261      751.0010
date 03-12-16      time 16:03      2
pHc(init) 5.45      DET pH      B-100.05
smpl size 5.054 g      id 1      665914
EP1      0.461 ml      4.64
ALKLINI 0.009 meq/g
```

Figure 2. Typical Report Printout Showing a Trimethylamine Titration

Validation data

This method was validated using batches of Aldisol (aldicarb technical solution) and trimethylamine analytical standard.

Precision: CV = 0.20%
(CV = relative standard deviation, obtained by threefold analysis)

Accuracy: 90.0%

Limit of detection: 0.002%

Limit of quantitation 0.005%

Approvals

Written By: *Sarah J. Leibowitz*
S. J. Leibowitz- Sr. Analytical Chemist

Approved By: *Stephen C. Stahck*
S. C. Stahck- Manager, NAFTA Analytical Services

Cross-References

Reference	Reference Title
SOP-0011	Calibration and maintenance of titrators and pH meters
PC07	Fee Code
CM-168	Aventis- Percentage Trimethylamine (TMA) by Titration

Bayer CropScience



STUDY TITLE

HPLC Determination of Aldicarb Impurities

Data Requirement

OECD Guidelines for Testing of Chemicals, Section 1 – Physical-Chemical Properties
EC Guidelines Part A – Methods for the Determination of Physico-Chemical Properties
EPA OPPTS Harmonized Test Guidelines Series 830 Product Properties Test
Guidelines

AUTHOR

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STUDY COMPLETION DATE

2004-02-26

PERFORMING LABORATORY

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SUBMITTING LABORATORY STUDY NUMBER

03S003

BAYER REPORT NO.

G200968



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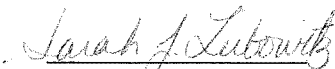
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Quality Assurance Statement

Not applicable.


Approvals Page

Study director:
Bayer CropScience


Dr. S. J. Leibowitz


March 1, 2004
Date

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Bayer CropScience:


S. C. Slahck

March 1, 2004
Date

Submitter:
Bayer CropScience


S. C. Slahck

March 1, 2004
Date

Confidentiality Statement

This report is confidential. No part of the report or any information contained therein may be disclosed to any third party without the prior written authorization of Bayer CropScience.

HPLC Determination of Aldicarb Impurities

Scope

This method is applicable to the determination of Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret in Aldisol™ (aldicarb technical solution).

Principle

Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret are determined by comparing the peak areas for the sample with corresponding standards of known percentage purity using acetanilide as an internal standard.

Reagents

<i>Reagent</i>	<i>Requirements</i>
Aldicarb nitrile	Analytical standard of known percentage purity (P ₁)
Aldicarb oxime	Analytical standard of known percentage purity (P ₂)
Acetanilide	Acros # AC15081-2500 or equivalent
Acetanilide, 0.003% (v/v) in methanol	Internal Standard Solution: Prepare by weighing 0.03 g of acetanilide into a bottle containing 1 L of methanol.
1,3-Dimethylurea	Analytical standard of known percentage purity (P ₃)
Methanol:water, 15:85	Mobile Solvent A: Prepare by adding 150 mL of methanol to a bottle or flask containing 850 mL of deionized water. Mix the contents well. Add a few glass beads and degas the solvent mixture under a vacuum source while sonicating.
Methanol:water, 30:70	Mobile Solvent B: Prepare by adding 300 mL of methanol to a bottle or flask containing 700 mL of deionized water. Mix the contents well. Add a few glass beads and degas the solvent mixture under a vacuum source while sonicating.
1,3,5-Trimethylbiuret	Analytical standard of known percentage purity (P ₄)
Water	Deionized

Aldisol is a trademark of Bayer CropScience

Equipment

<i>Equipment</i>	<i>Requirements</i>
Bath	Ultrasonic
HPLC Column	250 x 4.6-mm ID Zorbax Rx-C ₈ (5- μ m). Zorbax part # 880967 or equivalent.
Laboratory Data System	Waters Empower or equivalent
Liquid Chromatograph	Hewlett-Packard Model 1050 equipped with a variable wavelength detector, autoinjector, or equivalent equipment
Needle	Becton Dickinson Gauge 23G1
Syringe	1-mL, glass

Procedure

Danger: Aldicarb is an extremely toxic material. Proper PPE must be worn when handling samples. All sample preparation must be performed in a fume hood.

1. Set the following conditions on the instrument (different instruments may require slightly different conditions):

<i>Parameter</i>	<i>Value</i>	<i>Units</i>
Detector range ¹	1.0	V
Flow ²	1.7	mL/minute
Detector response ¹	1	sec
Injection volume	10	μ L
Stop time	30	minutes
Range	2.0	AUFS
Wavelength	205	nm
Solvents		
	A	Mobile Phase A
	B	Mobile Phase B
Solvent Program		
	Time, Minutes	%B
	Initial	0
	7.5	0
	8.5	100
	26.0	100
	27.0	0

¹Set these parameters using Control 11 and Control 7, respectively.

²Adjust the flow and solvent program as necessary to obtain resolution as shown in Figure 1.

2. Before injecting, pump mobile solvent through the column until the baseline becomes stable.
3. To prepare the impurities standard solution, weigh 0.014 – 0.016 \pm 0.0001 g (W_1) of Aldicarb Nitrile, 0.0008 – 0.0015 g \pm 0.0001 g (W_2) of Aldicarb Oxime, 0.004 – 0.008 \pm

0.0001 g (W_3) of 1,3-dimethylurea, and 0.004 – 0.008 g \pm 0.0001 g (W_4) of 1,3,5-trimethylbiuret analytical standards into a single 1/2-oz. bottle.

4. Pipet 10.0 mL of internal standard solution into the standard bottle from Step 3 and bottles to prepare all sample solutions in Step 5.
5. Using a glass syringe attached to a needle, measure ca. 0.5 - 0.7 mL of sample. Tare the balance. Transfer the entire syringe contents to the 1/2-oz. sample bottle. Return the empty syringe to the balance. Record the weight \pm 0.0001 g (W) of sample.
6. Cap and shake the bottles from Steps 4 and 5 vigorously to mix.
7. Inject the standard solution from Step 6 in duplicate. Record the peak areas of the acetanilide, Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret peaks as I, S_1 , S_2 , S_3 , and S_4 , respectively. Compare the internal standard:component peak area ratios, R_n , for each injection. The ratios must agree within 5.0% ($\pm 2.5\%$ of their average), otherwise, reinject the standard solution until 2 successive injections do agree. Figure 1 shows a typical standard chromatogram and Figure 3 lists typical computer parameters.
8. Inject each sample solution from Step 6 once. Record the peak areas for acetanilide, Aldicarb Nitrile, Aldicarb Oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret as B and A_1 , A_2 , A_3 , and A_4 respectively. A typical sample chromatogram is shown in Figure 2.
9. Inject the standard solution again after every 5 – 6 samples and again at the end of the run. Bracketing standards must meet the agreement criterion in Step 7.

Calculations:

$$R_n = \frac{I}{S_n} \quad M = \frac{A_n}{B} \quad K_n = W_{Sn} \times P_n \times \bar{R}_n$$

$$\text{Analyte } n, \% = \frac{K_n \times M_n}{W}$$

Symbol	Description
A	Peak area of component n in the sample chromatogram
B	Peak area of the internal standard for the sample chromatogram
I	Peak area of the internal standard for the standard chromatogram
P	Purity percentage of component n in the standard
S	Peak area of component n in the standard chromatogram
W	Sample weight, grams
W_s	Standard weight, grams

- Where n =
- 1 For Aldicarb Nitrile
 - 2 For Aldicarb Oxime
 - 3 For 1,3-dibutylurea
 - 4 For 1,3,5-trimethylbiuret

Chromatograms:

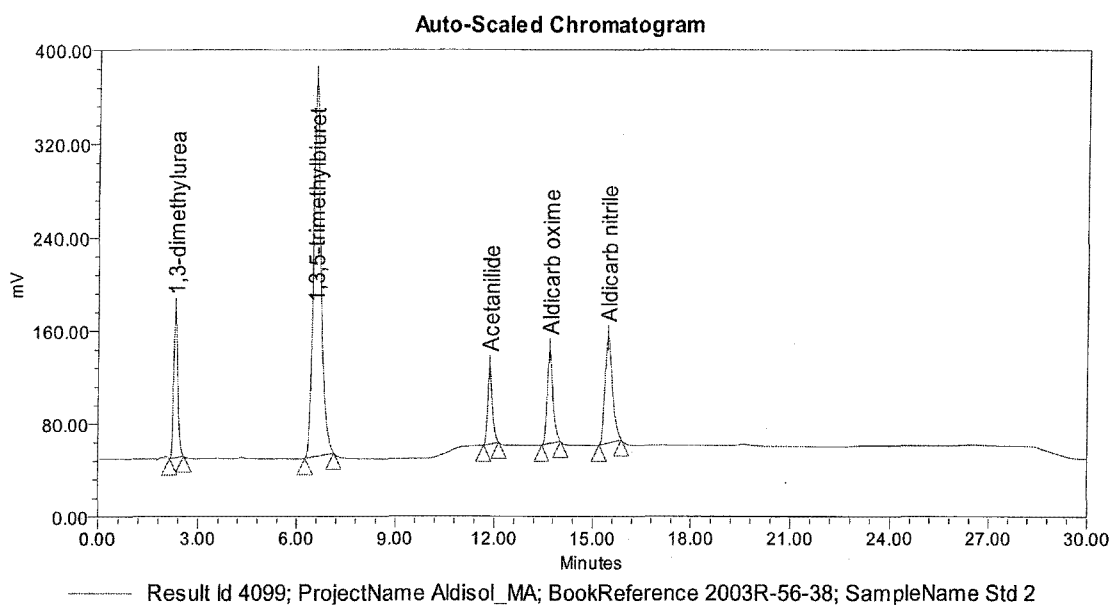


Figure 1. Typical Standard Chromatogram.

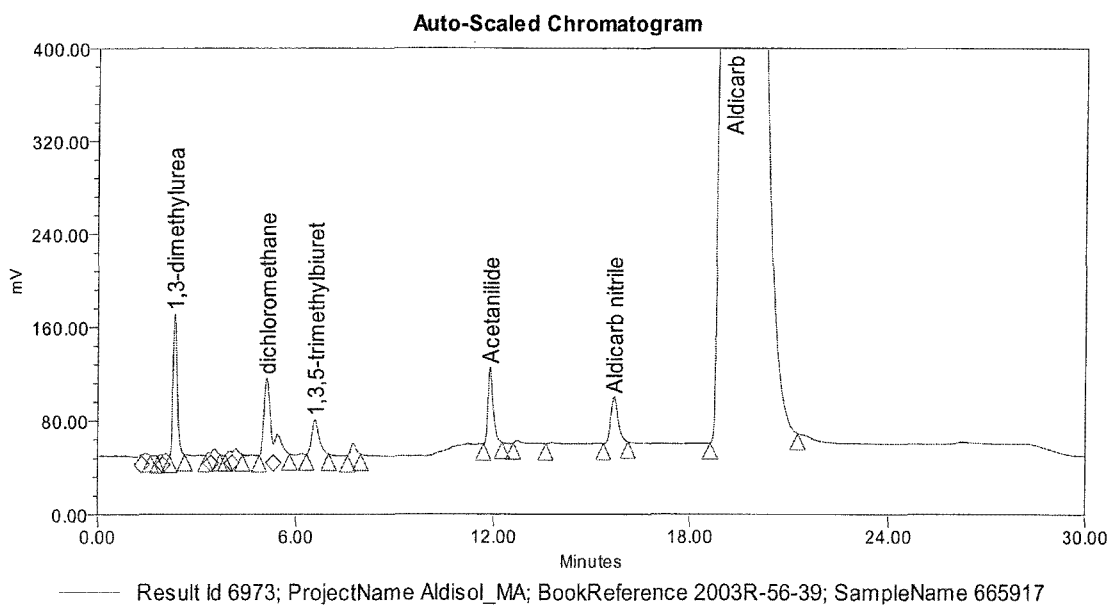


Figure 2. Typical Sample Chromatogram

Processing Parameters**Integration Parameters**

<i>Parameter</i>	<i>Units</i>	<i>Value</i>
Minimum Area	$\mu\text{V}*\text{sec}$	5000
Minimum Height	μV	100
Threshold	$\mu\text{V}*\text{sec}$	100
Width	sec	20

Components

<i>Field</i>	<i>Value</i>
RT Window %	5
Update RT	Never

<i>Name</i>	<i>Retention Time, minutes</i>	<i>Retention Time Window</i>	<i>Y Value</i>	<i>Internal Standard</i>	<i>Default Units</i>	<i>CcompRef1</i>
1,3-dimethylurea	2.3	0.125	Area	Acetanilide	%	
1,3,5-Trimethylbiuret	6.6	0.330	Area	Acetanilide	%	
Acetanilide	11.8	.590	Area			
Aldicarb Oxime	13.6	.770	Area	Acetanilide	%	
Aldicarb Nitrile	15.3	.850	Area	Acetanilide	%	
Aldicarb	21.0	.950	Area			

Default Amounts

<i>Level</i>	<i>1,3-Dimethylurea</i>	<i>1,3,5-trimethylbiuret</i>	<i>Acetanilide</i>	<i>Aldicarb Oxime</i>	<i>Aldicarb Nitrile</i>
Purity	99.2	99.7	100	99.1	99.0
Combo Factor	1	1	1	1	1
Multiple Standard Weights	1	1	1	1	1

Figure 3. Typical Computer Parameters.

Validation data

This method was validated using batches of Aldisol (aldicarb technical solution) and aldicarb nitrile, aldicarb oxime, 1,3-dimethylurea, and 1,3,5-trimethylbiuret Analytical standards.

Precision:	Aldicarb Nitrile: CV=0.02% Aldicarb Oxime: CV= N/A 1,3-Dimethylurea: CV = 0.02% 1,3,5-Trimethylbiuret: CV = 0.03% (CV = relative standard deviation, obtained by threefold analysis)
Linearity range:	Aldicarb Nitrile: 20 – 200% (w/w) Aldicarb Oxime: 20 – 200% (w/w) 1,3-Dimethylurea: 20 – 200% (w/w) 1,3,5-Trimethylbiuret: 20 – 200% (w/w) (of the nominal Analyte concentration) Acetanilide (internal standard): 20 – 200% (w/w) (of the nominal acetanilide concentration)
Working range:	Aldicarb Nitrile: 0.29 - 2.9 mg/mL Aldicarb Oxime: 0.07 - 0.7 mg/mL 1,3-Dimethylurea: 0.12 - 1.2 mg/mL 1,3,5-Trimethylbiuret: 0.14 - 1.4 mg/mL (of the component in solution) Acetanilide: 0.87 – 8.7 mg/100 mL (of the component in solution)
Accuracy:	Aldicarb Nitrile : 113% Aldicarb Oxime: N/A 1,3-Dimethylurea: 97.7% 1,3,5-trimethylurea: 117% (based on the analysis of a standard addition to Aldisol sample)
Limit of detection:	Aldicarb Nitrile 0.02% Aldicarb Oxime 0.02% 1,3-Dimethylurea 0.01% 1,3,5-Trimethylbiuret 0.01%
Limit of quantification:	Aldicarb Nitrile 0.04% Aldicarb Oxime 0.04% 1,3-Dimethylurea 0.02% 1,3,5-Trimethylbiuret 0.02%
Specificity:	The specificity is demonstrated by no interference from reagent blanks or internal standard. Sufficient separation of impurities and the internal standard are demonstrated in the chromatogram, Figure 2.
Stability:	The reference solution and sample solution are stable for at least 24 hours at ambient temperature.

Approvals

Written By:

Sarah J. Leibowitz
S. J. Leibowitz - Sr. Analytical Chemist

Approved By:

Stephen C. Slahck
S.C. Slahck - Manager, NAFTA Analytical Services

Cross-References

Reference	Reference Title
TM A-54.11	General Procedure for Waters Empower Laboratory Automation System
CM-9052	Aventis - Aldicarb Purity by HPLC; 6-1-2003
LC04	Fee Code