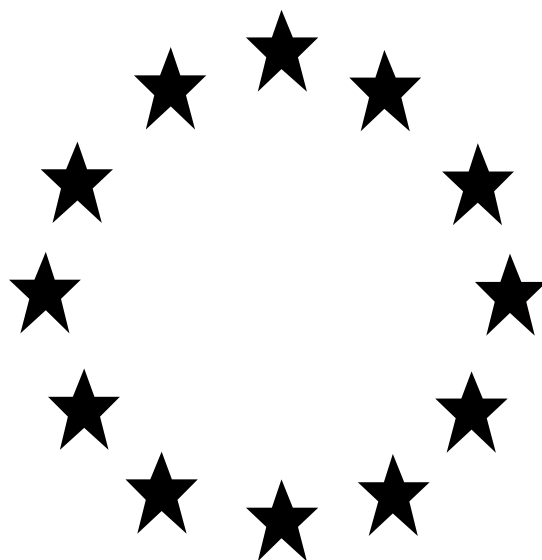




Draft Assessment Report (DAR)

- public version -

**Initial risk assessment provided by the rapporteur Member State
The Netherlands for the existing active substance**

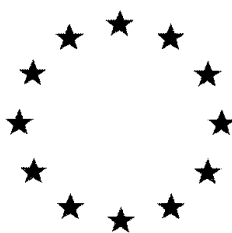
DICHLOBENIL

**of the third stage (part B) of the review programme
referred to in Article 8(2) of Council Directive 91/414/EEC**

Volume 3, Annex B, part 1, B.1 – B.5

January 2008

European Commission



DICHLOBENIL

VOLUME 3
Annex B

Rapporteur Member State: The Netherlands

April 2007

Draft Assessment Report and Proposed Decision of the Netherlands prepared in the context of the possible inclusion of dichlobenil in Annex I of Council Directive 91/414/EEC

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B.1 IDENTITY

B.1.1 IDENTITY OF THE ACTIVE SUBSTANCE (ANNEX IIA 1 AND 3.1)

All points of Annex IIA, Section 1 are addressed in Volume 1, Level 1.

B.1.2 IDENTITY OF THE PLANT PROTECTION PRODUCT (ANNEX IIIA 1)

All points of Annex IIIA, Section 1 are addressed in Volume 1, Level 1, and (for the confidential information) in Volume 4, Annex C.

B.1.3 REFERENCES RELIED ON

Section B.1 Identity (Annex IIA, point 1 and 3, Annex IIIA, point 1)

See Volume 4, Annex C (confidential information).

B.2 PHYSICAL AND CHEMICAL PROPERTIES

B.2.1 PHYSICAL AND CHEMICAL PROPERTIES OF THE ACTIVE SUBSTANCE (ANNEX IIA 2)

The physical and chemical properties of the active substance Dichlobenil are summarised in table B.2.1a). Moreover, information about some physical and chemical properties of the main metabolite 2,6-dichlorobenzamide (BAM) were submitted, which are summarised in table B.2.1b).

Table B.2.1a) Summary of the physical and chemical properties of the active substance Dichlobenil

Section (Annex point)	Study	Purity, Batch number	Method	Results	Comment	Reference
B.2.1.1 (IIA 2.1)	Melting point	pure 99.8% batch no. 020927	EEC A.1 (Thomas-Hoover melting point apparatus)	144 -145°C	-	Dunn, 2004 (GLP)
B.2.1.2 (IIA 2.1)	Boiling point	analytical grade 100% batch no. ARS9108BA	OECD103 (equivalent to the prescribed method EEC A.2). (Differential Scanning Calorimetry)	Dichlobenil melted, sublimed and evaporated. Boiling was not observed (tests were carried out at 98.86 kPa).	-	Malinski, 1999 (GLP)
B.2.1.3 (IIA 2.1)	Temperature of decomposition or sublimation	analytical grade 100% batch no. ARS9108BA	OECD103 (Differential Scanning Calorimetry)	Sublimation onset temperature was 120 °C at 98.86 kPa.	-	Malinski, 1999 (GLP)
B.2.1.4 (IIA 2.2)	Relative density	purified 100% batch no. ARS9108BA	EEC A.3 (Pycnometer)	$D_{4}^{20}=1.55$	-	Chee-Chue, 2001
B.2.1.5 (IIA 2.3)	Vapour pressure	purified 100% batch no. ARS9108BA	EEC A.4 (gas saturation method)	$1.4 \cdot 10^{-1}$ Pa at 25 °C	-	Tremain, 2001a (GLP)
B.2.1.6 (IIA 2.3)	Volatility, Henry's law constant	Not applicable	Calculation	$1.317 \text{ Pa} \cdot \text{m}^3 \cdot \text{mol}^{-1}$ at 25 °C	Calculated by the RMS (converted from value expressed as $\text{atm} \cdot \text{m}^3 \cdot \text{g} \cdot \text{mol}^{-1}$)	Summary document M-II

Table B.2.1a) Summary of the physical and chemical properties of the active substance Dichlobenil

Section (Annex point)	Study	Purity, Batch number	Method	Results	Comment	Reference
B.2.1.7 (IIA 2.4)	Appearance: physical state of purified active substance	purified 100% batch no. ARS9108BA	OPPTS 830.6303 (visual)	Needle shaped, crystalline solid (approximately 2 mm in length).	-	Chee-Chue, 2002 (GLP)
B.2.1.7 (IIA 2.4)	Appearance: physical state of technical grade active substance	technical 98.7% batch no. FUE97H07A	OPPTS 830.6303 (visual)	Sticky solid.	-	Chee-Chue, 2002 (GLP)
B.2.1.8 (IIA 2.4)	Appearance: colour of purified active substance	purified 100% batch no. ARS9108BA	OPPTS 820.6302 (visual)	White. (Munsell notation: N 9.25/.)	-	Chee-Chue, 2002 (GLP)
B.2.1.8 (IIA 2.4)	Appearance: colour of technical grade active substance	technical 98.7% batch no. FUE97H07A	OPPTS 820.6302 (visual)	White. (Munsell notation: N 9.73/.)	-	Chee-Chue, 2002 (GLP)
B.2.1.9 (IIA 2.4)	Appearance: odour of purified active substance	purified 100% batch no. ARS9108BA	OPPTS 820.6304 (olfactory perception)	Musty.	-	Chee-Chue, 2002 (GLP)
B.2.1.9 (IIA 2.4)	Appearance: odour of technical grade active substance	technical 98.7% batch no. FUE97H07A	OPPTS 820.6304 (olfactory perception)	Musty.	-	Chee-Chue, 2002 (GLP)

Table B.2.1a) Summary of the physical and chemical properties of the active substance Dichlobenil

Section (Annex point)	Study	Purity, Batch number	Method	Results	Comment	Reference
B.2.1.10 (IIA 2.5)	Spectra of purified active substance	purified 100% batch no. ARS9108BA	94/37/EC, Annex I, Section 2.5	The following spectra are submitted: UV/vis, IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and MS. UV molar absorbance coefficient ϵ (L/mol.cm) of 1985.3 at 298.9 nm, 1878.8 at 290 nm, 5766.9 at 243 nm, 6805.9 at 236.9 nm and 38528.8 at 211 nm. IR spectrum shows the stretching frequency for the aromatic CH groups at 3090.9 cm^{-1} and the CN group at 2220.09 cm^{-1}. $^1\text{H-NMR}$ spectrum shows chemical shift values at 7.416-7.510 (3H,m). $^{13}\text{C-NMR}$ spectrum shows chemical shift values at 113.560 (carbon of the nitrile group), 114.694 (carbon attached to the nitrile group), 128.380 (two aromatic carbons in meta position), 134.053 (aromatic carbon in para position), 138.750 (two aromatic carbons each bonded to chlorine). MS spectrum shows the molecular ion at m/z 171 and characteristic ion fragments at m/z 136 and 100.	-	Hull, 2003 (GLP)
B.2.1.11 (IIA 2.6)	Solubility in water of technical grade active	technical 99.1% batch no. FUN85118A	OECD105 (flask method with UV determination)	21 mg/L at 25 °C	non GLP study, but considered scientifically valid and therefore accepted for evaluation	van Berkel, de Kok, Olthof, 1987 (non GLP)

Table B.2.1a) Summary of the physical and chemical properties of the active substance Dichlobenil

Section (Annex point)	Study	Purity, Batch number	Method	Results	Comment	Reference
	substance	analytical grade 99.5% batch no. ARS82101N	OECD105 (flask method with UV determination)	pH 5: 20.5 mg/L at 25 °C pH 7: 21.2 mg/L at 25 °C pH 9: 21.9 mg/L at 25 °C	-	van Berkel, Olthof, 1988 (GLP)
B.2.1.12 (IIA 2.7)	Solubility in organic solvents (technical active substance)	technical 99.1% batch no. FUN85118A	OECD105 (flask method with UV determination)	xylene 53 g/L at 25 °C ethanol 15 g/L at 25 °C cyclohexane 3.7 g/L at 25 °C	non GLP study, but considered scientifically valid and therefore accepted for evaluation	van Berkel, de Kok, Olthof, 1987 (non GLP)
		technical 99.1% batch no. FUN85118A	GC analysis of saturated solutions	acetone 86 g/L at 20 °C methanol 17.2 g/L at 20 °C dichloromethane 151 g/L at 20 °C	-	Riggs, Buckrell, 1999 (GLP)
		technical 99.1% batch no. FUN95C10A	OECD105 (flask method with GC determination)	ethylacetate 59.3 g/L at 20 °C	-	O'Connor, Mullee, 2000 (GLP)
B.2.1.13 (IIA 2.8)	Partition coefficient of technical active substance	technical 99.8% batch no. FUX003000/FUN82 B07A	OECD proposal; document PC 84.1 (HPLC method)	pH 3: 2.7 at 22°C	non GLP study, but considered scientifically valid and therefore accepted for evaluation; the method used is equivalent to the current HPLC method of EEC A.8	Thus, 1985 (pre GLP)
B.2.1.14 (IIA 2.9)	Stability in water	> 99.5% batch no. ARS 53078-1	BBA Merkblatt no. 55	Test duration 150 d at 22 ± 1°C pH 5: > 150 days pH 7: > 150 days pH 9: > 150 days	not acceptable due to various shortcomings	Buisman, 1988 (GLP)
B.2.1.15 (IIA 2.9)	Hydrolysis rate	> 99.5% batch no. ARS 53078-1	BBA Merkblatt no. 55	Based on the data reported under B.2.1.4, Dichlobenil is considered hydrolytically stable at environmentally relevant pH's.		Van Oevelen, 2005 (addendum to Buisman, 1987)

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Table B.2.1a) Summary of the physical and chemical properties of the active substance Dichlobenil

Section (Annex point)	Study	Purity, Batch number	Method	Results	Comment	Reference
B.2.1.16 (IIA 2.9)	Photochemical degradation	Radiolabel [^{14}C] radiochemical purity: 99.3% Chemical purity 98.3% batch no. AO187L04A	EPA 161-2	DT50 at 25°C: Xenon light: 15.1 days Natural sunlight: 10.2 days	-	Boelhouwers, Joustra, Klein, Stegman, 1989 (GLP)
B.2.1.17 (IIA 2.9)	Quantum yield (water)	Purity, batch: not applicable	Calculation	1.5E-03 mol/einstein	-	Harned, 2003a, Harned, 2003b (GLP)
B.2.1.18 (IIA 2.9)	Dissociation constant (pK_a)	analytical grade 100% batch no. ARS9108BA	OECD 112 (spectrophotometric assessment at 20 °C)	Spectra of solutions over the pH range 2-12 exhibited no significant differences indicating that the substance does not undergo dissociation under the test conditions	-	Malinski, 1999 (GLP)
B.2.1.19 (IIA 2.10)	Stability in air, photochemical oxidative degradation	Purity, batch: not applicable	AOPWIN (theoretical approach)	At a hydroxyl concentration of 1.56×10^6 molecules/ cm^3 the DT50 is 63 days, assuming 12 hour light per day. The overall rate constant is 0.1704 E-12 $\text{cm}^3/\text{molecule} \cdot \text{sec}$.	-	Schocken, 2001 (GLP)
B.2.1.20 (IIA 2.11)	Flammability and auto-flammability (technical active substance)	technical 99.3% batch no. AS 26945 SI 7812	EEC A.10	Not highly flammable	-	Tremain, 2001b (GLP)
B.2.1.21 (IIA 2.12)	Flash point (technical active substance)	technical 99.3% batch no. AS 26945 SI 7812	EEC A.16	No relative self-ignition temperature below its melting temperature.	-	Tremain, 2001b (GLP)
		-	-	Not applicable.	Non-determination is acceptable because the a.s. is a solid and its melting point is not below 40 °C.	-

Table B.2.1a) Summary of the physical and chemical properties of the active substance Dichlobenil

Section (Annex point)	Study	Purity, Batch number	Method	Results	Comment	Reference
B.2.1.22 (IIA 2.13)	Explosive properties (technical active substance)	technical 99.1% batch no. W05-30767 CH73-95	EEC A.14 (thermal sensitivity, shock, friction)	Not explosive.	-	Krips, 1995a (GLP)
B.2.1.24 (IIA 2.14)	Surface tension	technical 99.3% batch no. AS 26945 SI 7812	EEC A.5 (ISO 304 ring method)	68.5 mN/m (1.58·x10 ⁻² g/L solution) at 20 °C	-	Evans, 2001 (GLP)
B.2.1.23 (IIA 2.15)	Oxidising properties (technical active substance)	technical 99.1% batch no. W05-30767 CH73-95	EEC A.17 test	Not oxidizing.	-	Krips, 2001b (GLP)

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Table B.2.1b) Summary of the physical and chemical properties of the main metabolite BAM

Section (Annex point)	Study	Purity, Batch number	Method	Results	Comment	Reference
B.2.1.5 (IIA 2.3)	Vapour pressure of main soil metabolite	2,6-dichloro-benzamide analytical grade 99.7% batch no. ARS81C25N	OPPTS 830.7950 OECD104 (equivalent to the prescribed method EEC A.4) (gas saturation method)	$\leq 2 \cdot 10^{-5}$ Pa at 25 °C		Riggs, 2000a (GLP)
B.2.1.10 (IIA 2.5)	Spectra of primary metabolite	2,6-dichloro-benzamide 97% batch no. 00 1B97 0001	91/414/EEC, Annex II, Section 2.5.1 OPPTS 830.7050 OECD101	The following spectra are submitted: UV/vis, IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and MS (in methanol). Spectra confirm structure for 2,6-dichlorobenzamide (absorption coefficients are not reported).	-	Bowen, 2003 (GLP)
B.2.1.11 (IIA 2.6)	Solubility in water of metabolite	2,6-dichloro-benzamide analytical grade 99.7% batch no. ARS81C25N	OECD105 and EEC A.6 (flask method with HPLC determination)	pH 6: 1.83 g/L at 20 °C	-	Riggs, 2000b (GLP)
B.2.1.13 (IIA 2.8)	Partition coefficient of main metabolite	2,6-dichlorobenzamide purity and batch number not given	OECD proposal; document PC 84.1 (HPLC method)	pH 3: 0.38 at 22 °C	-	Thus, 1985 (GLP)
		2,6-dichlorobenzamide analytical grade 99.7% batch no. ARS81C25N	OECD 117 (HPLC with UV detector)	0.51	The pH and temperature are not reported.	Riggs, 2000c (GLP)

Table B.2.1b) Summary of the physical and chemical properties of the main metabolite BAM

Section (Annex point)	Study	Purity, Batch number	Method	Results	Comment	Reference
B.2.1.15 (IIA 2.9)	Hydrolysis rate	[¹⁴ C]-2,6-dichlorobenzamide 99% batch no. SEL/1169	EPA 161	At 50°C and at 25 °C for 5 days hydrolytically stable at pH 4,7 and 9 (<1.2% unidentified metabolites)	-	Jacob and Fitzmaurice, 2003 (GLP)
B.2.1.18 (IIA 2.9)	Dissociation constant (pK _a)	2,6-dichlorobenzamide Purity, batch: not applicable	OPPTS 830.7370; (calculation/discussion)	No dissociation expected at environmentally relevant pHs.	-	White, 2000

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B.2.2 PHYSICAL, CHEMICAL AND TECHNICAL PROPERTIES OF THE PLANT PROTECTION PRODUCT (ANNEX IIIA 2)

Table B.2.2 Summary of the physical and chemical properties of the plant protection product - Product name: Casoron® G

Section (Annex point)	Study	Method	Results	Comment	Reference
B.2.2.1 (IIIA 2.1)	Appearance: physical state	Visual	Free flowing granules.	-	Brown, 2003 (GLP)
B.2.2.2 (IIIA 2.1)	Appearance: colour	Visual	Grey. (Munsell notation: 4.8Y 6.4/1.6)	-	Brown, 2003 (GLP)
B.2.2.3 (IIIA 2.1)	Appearance: odour		Aromatic.	-	Brown, 2003 (GLP)
B.2.2.4 (IIIA 2.2)	Explosive properties	Statement	Not explosive.	The EEC A.14 method (explosive properties) was replaced by a theoretical statement, which is acceptable.	van der Baan-Treur, 2003a (GLP)
B.2.2.5 (IIIA 2.2)	Oxidising properties	Statement	Not oxidizing.	The EEC A.17 method (oxidizing properties) was replaced by a theoretical statement, which is acceptable.	van der Baan-Treur, 2003b (GLP)
B.2.2.6 (IIIA 2.3)	Flammability	EEC A.10	Not highly flammable.	-	Schuurman, 1988 (GLP)
B.2.2.7 (IIIA 2.3)	Auto-flammability	EEC A.16	Not auto-flammable up to 400°C.	-	Schuurman, 1988 (GLP)
B.2.2.8 (IIIA 2.3)	Flash point	-	Only required for liquids.	Non-determination is acceptable	-
B.2.2.9 (IIIA 2.4)	Acidity/alkalinity	-	Not applicable because the product is not acidic (pH<4) or alkaline (pH>10).	Non-determination is acceptable	-
B.2.2.10 (IIIA 2.4)	pH	-	Not applicable because the product will not be applied as an aqueous dilution.	Non-determination is acceptable	-
B.2.2.11 (IIIA 2.5)	Surface tension	-	Not applicable because the product is not a liquid.	Non-determination is acceptable	-

Table B.2.2 Summary of the physical and chemical properties of the plant protection product - Product name: Casoron® G

Section (Annex point)	Study	Method	Results	Comment	Reference
B.2.2.12 (IIIA 2.5)	Viscosity	-	Not applicable because the product is not a liquid preparation for ultra low volume use and not a non-newtonian liquid.	Non-determination is acceptable	-
B.2.2.13 (IIIA 2.6)	Relative density	-	Not applicable because the product is not a liquid.	Non-determination is acceptable	-
B.2.2.14 (IIIA 2.6)	Bulk (tap) density	BAI 40 506, Engelsmann method	Bulk density $E_0 = 1.10 \pm 0.02$ g/mL Tap density $E_{100} = 1.17 \pm 0.02$ g/mL No apparent change in the bulk and tap density is observed after storing the product for 3 years under warehouse conditions.	The principle of the Engelsmann method is as follows: a measuring cylinder is filled with granules. Volume and weight are recorded from which the bulk density can be calculated. Tap density is determined following a standardized number of tappings.	Poel, 2004 (GLP)
B.2.2.14 (IIIA 2.7)	Storage stability	Method BAI 41 003	Average content at start: 6.63% Average content at end: 6.57% The content of Dichlobenil in the product remains stable during accelerated storage testing (14 days at 54 °C).	Method BAI 41 003 is a gas chromatographic determination of 2,6-dichlorobenzonitril in formulations. This method is similar to the validated method GRL-GM-1117.	Poel, 2004 (GLP)

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Table B.2.2 Summary of the physical and chemical properties of the plant protection product - Product name: Casoron® G

Section (Annex point)	Study	Method	Results	Comment	Reference
B.2.2.15 (IIIA 2.7)	Shelf life	GIFAP Monograph no. 17	Average content at start: 6.66% Average content at end: 6.68% No apparent decrease in the percentage of the active ingredient after three years of storage under ambient warehouse conditions in the absence of direct sunlight. No colour change. No visual differences in the state of the packing (inside) after three years of storage. Packing was a cardboard box containing an aluminium lined paper bag, fit to contain 5 kg of product. The shelf life is at least 3 years.	Results before and after storage are also reported under B.2.2.14. These results are also relevant in relation to the shelf life.	Poel, 2004 (GLP)
B.2.2.16 (IIIA 2.8)	Wettability	-	Not applicable because the product is not a preparation that is diluted for use.	Non-determination is acceptable	-
B.2.2.17 (IIIA 2.8)	Persistent foaming	-	Not applicable because the product is not a preparation that is diluted for use.	Non-determination is acceptable	-
B.2.2.18 (IIIA 2.8)	Suspensibility	-	Not applicable because the product is not a water dispersible product.	Non-determination is acceptable	-
B.2.2.19 (IIIA 2.8)	Suspension stability	-	Not applicable because the product is not a water dispersible product.	Non-determination is acceptable	-
B.2.2.20 (IIIA 2.8)	Dilution stability	-	Not applicable because the product is not a water soluble product.	Non-determination is acceptable	-
B.2.2.21 (IIIA 2.8)	Dry sieve test	-	Not applicable because the product is not a dustable powder.	Non-determination is acceptable	-
B.2.2.22 (IIIA 2.8)	Wet sieve test	-	Not applicable because the product is not a water dispersible product.	Non-determination is acceptable	-

Table B.2.2 Summary of the physical and chemical properties of the plant protection product - Product name: Casoron® G

Section (Annex point)	Study	Method	Results	Comment	Reference
B.2.2.23 (IIIA 2.8)	Particle size distribution	BAI 40 516	>2.0 mm 0% 1.25-2.0 mm <4% 1.0-1.25 mm <25% 0.5-1.0 mm >60% 0.25-0.5 mm >10% 0.1-0.25 mm <0.1% <0.1 mm <0.1% Number of particles/gram 2500-3000 The nominal size of the granules does not undergo any apparent changes during three years storage under warehouse conditions.	A quantity of sample material is mechanically sieved for a particular time in a number of sieves stacked one on top of the other, after which the separate fractions are determined by weighing. The number of particles per gram of compacted granule is calculated from the sieve fractions.	Poel, 2004
B.2.2.24 (IIIA 2.8)	Content of dust/fines	CIPAC Method MT 171	Dust content at start: 0.3 mg Dust content at end (3 years): 0.2 mg The product is nearly dust-free (category 1 of CIPAC Method MT 171).	-	Poel, 2004
B.2.2.25 (IIIA 2.8)	Attrition and friability	BAI 40 515	Friability at start: 6.4-6.7% Friability at end: 5.1-5.3% The friability (attrition characteristics) does not deteriorate over a 3-years storage interval at ambient warehouse conditions.	The attrition of granules is determined from the increase in the dust content using a ball mill.	Poel, 2004
B.2.2.26 (IIIA 2.8)	Emulsifiability, re-emulsifiability and emulsion stability	-	Not applicable because the product does not form emulsions.	Non-determination is acceptable	Poel, 2004
B.2.2.27 (IIIA 2.8)	Stability of dilute emulsion	-	Not applicable because the product does not form emulsions.	Non-determination is acceptable	Poel, 2004
B.2.2.28 (IIIA 2.8)	Flowability	CIPAC Method MT 172	The flowability of the granules after 14 days storage at 54 °C under pressure (25 g/cm ³) is unaffected. The granules drop spontaneously through a 5 mm sieve.	-	Poel, 2004
B.2.2.29 (IIIA 2.8)	Pourability (rinsibility)	-	Not applicable because the product is not a suspension.	Non-determination is acceptable	-
B.2.2.30 (IIIA 2.8)	Dustability	-	Not applicable because the product is not a dustable powder.	Non-determination is acceptable	-

Table B.2.2 Summary of the physical and chemical properties of the plant protection product - Product name: Casoron[®] G

Section (Annex point)	Study	Method	Results	Comment	Reference
B.2.2.31 (IIIA 2.8)	Adherence and distribution to seeds	-	Not applicable because the product is not used for seed treatment.	Non-determination is acceptable	-
IIIA 2.9.1	Physical compatibility with other products	-	Not applicable because the product is a ready-to-go granular formulation and is not intended for tank-mixes.	Non-determination is acceptable	-
IIIA 2.9.2	Chemical compatibility with other products	-	Not applicable because the product is a ready-to-use granular formulation and is not intended for tank-mixes.	Non-determination is acceptable	-

WARNING: This document forms part of a dossier submitted in support of a registration application. It is not to be read in isolation. Registration must not be granted on the basis of this document.

B.2.3 Summary and evaluation of physical-chemical properties

active substance

Dichlobenil is a white, needle-shaped, crystalline solid (the purified substance) or a white sticky solid (the technical substance) with a musty odour. Its relative density (D_{4}^{20}) is 1.55. In a melting point apparatus a melting point of 144-145°C was observed, while Differential Scanning Calorimetry showed that the substance melted, sublimed and evaporated with a sublimation onset temperature of 120°C. Because the substance sublimes, no boiling point can be determined. The vapour pressure is 0.14 Pa at 25°C and the volatility (Henry's law constant) is $1.317 \text{ Pa} \cdot \text{m}^3 \cdot \text{mol}^{-1}$ at 25 °C.

Dichlobenil is hardly soluble in water (21 mg/L at pH 7 and 25 °C for the analytical grade material) and its partition coefficient ($\log P_{\text{ow}}$) is 2.7 at pH 3 and 22 °C. The surface tension of a 90% saturated solution in water at 20 °C is 68.5 mN/m, indicating that the compound is not surface active.

The solubility in various organic solvents is 53 g/L at 25°C in xylene, 15 g/L at 25°C in ethanol, 3.7 g/L at 25°C in cyclohexane, 86 g/L at 20°C in acetone, 17.2 g/L at 20°C in methanol, 151 g/L at 20°C in dichloromethane and 59.3 g/L at 20°C in ethylacetate.

The substance is not flammable and not self-ignitable. The substance has no explosive properties and no oxidizing properties.

The spectra provided agree with the structure for 2,6-dichlorobenzonitrile. The UV spectrum shows absorption maxima at 298.9 nm ($\epsilon = 1985.3$), 290 nm, 243 nm, 236.9 nm and 211 nm. The IR spectrum shows characteristic peaks at 3090.9 cm^{-1} and 2220.09 cm^{-1} . The ^1H -NMR spectrum shows chemical shift values at 7.416-7.510 (3H,m) and the ^{13}C -NMR spectrum at 113.560, 114.694, 28.380, 134.053 and 138.750. The mass spectrum shows the molecular ion at m/z 171 and characteristic ion fragments at m/z 136 and 100. No dissociation occurs over pH range 2 – 12.

The results of the investigation of the photochemical degradation at 25°C resulted in DT50 under Xenon light and natural sun light account for 15 and 10 days, respectively.

The quantum yield in water accounts for $1.5\text{E}-03 \text{ mol/einstein}$. The estimated half life of the photochemical oxidative degradation accounts for 63 days.

Additional remarks: The stability of Dichlobenil in water was investigated (Buisman, 1988 addended by Van Oevelen, 2005) however, due to various shortcomings of the performance and reporting of the test performance (e.g. recovery of the analytical method was not determined, test was carried out in non-sterile glass vessels, intended pH value of 5 showed a value of 7, pH values were only given for one occasion, metabolites were not determined, turbidity in buffered solutions, no GLP -unsigned statement), the study is not accepted for the overall evaluation. However, the available data are considered sufficient to elucidate the stability of Dichlobenil in water. Therefore, no additional data regarding this subject are requested.

In the reference list in Document M-II it is claimed that the studies on the solubility of Dichlobenil in water (van Berkel, de Kok, Olthof, 1987) and the determination of the partition coefficient of

Dichlobenil (Thus, 1985) were carried out under GLP conditions. However, this is not the case - by that time, GLP was not required. However, since the studies are considered scientifically valid they are used for the overall evaluation.

metabolite 2,6-dichlorobenzamide

The main metabolite in various environmental and biological matrices is 2,6-dichlorobenzamide (BAM). Some physical and chemical properties of BAM were therefore elucidated as well. The spectra for this substance are in agreement with the structure. This substance has a vapour pressure of less than $2 \cdot 10^{-5}$ Pa at 25 °C. Its solubility in water at 20 °C and pH 6 is 1.83 g/L and its partition coefficient (logPow) at 22 °C and pH 3 is 0.38. For the latter parameter, also 0.51 is reported, but the temperature and pH are not known. However, both values do not differ significantly. A study on the hydrolysis rate was submitted under IIA7.2.11. Here BAM was hydrolytically stable at 25°C and 50°C for 5 days at pH 4, 7 and 9. No dissociation is expected at relevant pHs (pH range 2 – 12).

plant protection product

Casoron® G is a grey-coloured, free-flowing granular product with an aromatic odour and containing 6.75% (w/w) of Dichlobenil. The content of Dichlobenil in the product remained stable during accelerated storage testing (14 days at 54 °C). There was also no apparent change in the percentage of the active ingredient after three years of storage under ambient warehouse conditions in the absence of direct sunlight. The bulk density is approximately 1.10 g/mL, while the tap density is approximately 1.17 g/mL. The nominal size of the granules did not undergo any apparent changes during three years storage under warehouse conditions. The friability (attrition characteristics) did not deteriorate over a 3-years storage interval at ambient warehouse conditions. The formulation is nearly dust-free. The flowability of the granules after 14 days storage at 54 °C under pressure (25 g/cm²) is unaffected. The shelf life time is at least three years under normal warehouse conditions. The formulation is not flammable and not self-ignitable. The formulation has no explosive properties and no oxidizing properties.

B.2.4 References relied on

Section B.2 Physical and chemical properties (Annex IIA, point 2, Annex IIIA, point 2)

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIA 2.1.1	Dunn, N.L.	2004	The melting point of Dichlobenil Crompton Co., Research Laboratories, Ontario, Canada Report no. GRL-12152 GLP, unpublished	Y	CHEM
IIA 2.1.2	Malinski, M.F.	1999	Dichlobenil – boiling point, thermal stability and dissociation constant Analytical Services Ricerca Inc., USA (Uniroyal Chemical Company) Report no. Doc. No. 011003-1, Proj. No. 99205 GLP, unpublished	Y	CHEM
IIA 2.1.3	Malinski, M.F.	1999	Dichlobenil – boiling point, thermal stability and dissociation constant Analytical Services Ricerca Inc., USA (Uniroyal Chemical Company) Report no. Doc. No. 011003-1, Proj. No. 99205 GLP, unpublished	Y	CHEM
IIA 2.2	Chee-Chue, L.C.	2001	Determination of the density of purified Dichlobenil Crompton Co., Research Laboratories, Ontario, Canada Report no. GRL-FR-11782 GLP, unpublished	Y	CHEM
IIA 2.3.1/01	Tremain, S.P.	2001a	Dichlobenil pure – determination of vapour pressure Safepharma Laboratories Ltd., United Kingdom Report no. 666/052 (Crompton Europe Ltd. No. 2001-113) GLP, unpublished	Y	CHEM
IIA 2.3.1/02	Riggs, A.S.	2000a	Vapour pressure of 2,6-dichlorobenzamide Uniroyal Chemical Research Laboratories, Ontario, Canada Report no. GRL-11494 GLP, unpublished	Y	CHEM

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIA 2.4	Chee-Chue, L.C.	2002	The colour, physical state and odour of technical and purified Dichlobenil (amended final report) Crompton Co., Research Laboratories, Ontario, Canada Report no. GRL-FR-11761-01 GLP, unpublished	Y	CHEM
IIA 2.5/01	Hull, L.B.	2002	UV/VIS, IR, NMR, and MS spectra of Dichlobenil Crompton Co. Crop Protection R&D, Middlebury, USA Report no. 2003-013 GLP, unpublished	Y	CHEM
IIA 2.5/02	Bowen, T.	2003	AE C653711: spectral data (UV/VIS, IR, ¹ H-NMR, ¹³ C-NMR, MS) Bayer Cropscience, Germany Report no. C038927 GLP, unpublished	Y	CHEM
IIA 2.6/01	van Berkel, M.P. de Kok, H.A.M. Olthof, J.A.	1987	Physical and chemical characteristics of dichobenil Duphar BV, The Netherlands Report no. 56630/244/1987 GLP, unpublished	Y	CHEM
IIA 2.6/02	van Berkel, M.P. Olthof, J.A.	1988	Solubility of Dichlobenil in water of pH 5.0, 7.0 and 9.0 at 298k Duphar BV, The Netherlands Report no. 56630/124/1988 GLP, unpublished	Y	CHEM
IIA 2.6/03	Riggs, A.S.	2000b	Solubility of 2,6-dichlorobenzamide in water Uniroyal Chemical Research Laboratory, Ontario, Canada Report no. GRL-FR-11493 GLP, unpublished	Y	CHEM
IIA 2.7/01	van de Berkel, M.P. de Kok, H.A.M. Olthof, J.A.	1987	Physical and chemical characteristics of dichobenil Duphar BV, The Netherlands Report no. 56630/244/1987 Non-GLP ¹ , unpublished	Y	CHEM

¹ GLP is claimed in the reference list in Document M-II, but this is not correct.

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIA 2.7/02	Riggs, A.S. Buckrell, H.M.	1999	Solubility of Dichlobenil technical in acetone, dichloromethane and methanol Uniroyal Chemical Research Laboratory, Ontario, Canada Report no. GRL FR-11582 GLP, unpublished	Y	CHEM
IIA 2.7/03	O'Connor, B.J. Mullee, D.M.	2000	Dichlobenil technical: determination of the solubility in ethyl acetate Safeparm Laboratories Ltd., United Kingdom Report no. 666/026 GLP, unpublished	Y	CHEM
IIA 2.8	Thus, J.L.G.	1985	Determination by HPLC of the log P value of Dichlobenil and its main metabolite Duphar BV, The Netherlands Report no. 56635/12/1985 Non-GLP ² , unpublished	Y	CHEM
II A 2.9/02	Jacob, O., Fitzmaurice, M	2003	[14C]-AE C653711: hydrolysis at pH 4, 5, 7 and 9 Report Battelle Agrifood Ltd., United Kingdom No.CX/03/030 CA - 4188 GLP, Unpublished	Y	CHEM
IIA 2.9.2/03	Boelhouwers, E.J. Joustra, K.D. Klein, G. Stegman, K.	1989	Photodegradation of [¹⁴ C]Dichlobenil in water Duphar BV, The Netherlands Report no. 56630/58/1989 GLP, unpublished	Y	CHEM
IIA 2.9.3/01	Harned, W.H.	2003a	Quantum yield calculation for Dichlobenil Crompton Co., Uniroyal Chemical Division, Middlebury, USA Report no. 2001-060 GLP, unpublished	Y	CHEM
IIA 2.9.3/02	Harned, W.H.	2003b	Calculation of the theoretical lifetime of Dichlobenil in upper surface waters Crompton Co., Uniroyal Chemical Division, Middlebury, USA Report no. 2001-157 GLP, unpublished	Y	CHEM

² GLP is claimed in the reference list in Document M-II, but this is not correct.

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIA 2.9.4/01	Malinski, M.F.	1999	Dichlobenil – boiling point, thermal stability and dissociation constant Analytical Services Ricerca Inc., USA (Uniroyal Chemical Company) Report no. Doc. No. 011003-1, Proj. No. 99205 GLP, unpublished	Y	CHEM
IIA 2.9.4/02	White, C.K.	2000	Dissociation constant of 2,6- dichlorobenzamide in water Witco Corporation, Uniroyal Chemical Division, USA Report no. 99243 GLP, unpublished	Y	CHEM
IIA 2.10	Schocken, M.J.	2001	Gas-phase oxidation rate and half-life of Dichlobenil in the troposphere Uniroyal Chemical Co., Inc., Middlebury, USA Report no. 2001-54 GLP, unpublished	Y	CHEM
IIA 2.11	Tremain, S.P.	2001b	Dichlobenil technical study report – determination of hazardous physico-chemical properties Safepharm Laboratories Ltd., United Kingdom Report no. 666/050 (Crompton Europe Ltd. No. 2001-075) GLP, unpublished	Y	CHEM
IIA 2.13	Krips, H.J.	1995a	Determination of the explosive properties of Dichlobenil technical Notox BV, The Netherlands Report no. 146262 GLP, unpublished	Y	CHEM
IIA 2.14	Evans, A.J.	2001	Dichlobenil technical study report – determination of surface tension Safepharm Laboratories Ltd., United Kingdom Report no. 666/051 (Crompton Europe Ltd. No. 2001-076) GLP, unpublished	Y	CHEM
IIA 2.15	Krips, H.J.	1995b	Determination of the oxidizing properties of Dichlobenil technical Notox BV, The Netherlands Report no. 146273 GLP, unpublished	Y	CHEM

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIIA 2.1	Brown, M.H.	2003	The appearance of Casoron G Crompton Co., Research Laboratories, Ontario, Canada Report no. GRL-11767 GLP, unpublished	Y	CHEM
IIIA 2.2.1	van der Baan- Treur, J.	2003a	Expert statement on the explosive properties of Casoron G Notox BV, The Netherlands Report no. 387528 GLP, unpublished	Y	CHEM
IIIA 2.2.2	van der Baan- Treur, J.	2003b	Expert statement on the oxidizing properties of Casoron G Notox BV, The Netherlands Report no. 387539 GLP, unpublished	Y	CHEM
IIIA 2.3	Schuurman, P.	1988	Flammability and autoflammability of Casoron G TNO, Rijswijk Report no. 294188237d GLP, unpublished	Y	CHEM
IIIA 2.6, IIIA 2.7, IIIA 2.8	Poel, E.N.	2004	A storage stability study of Casoron G; 3 years under warehouse conditions in original packaging Crompton Europe BV, The Netherlands Report no. 951/09/2003 GLP, unpublished	Y	CHEM

B.3 DATA ON APPLICATION AND FURTHER INFORMATION

B.3.1 DATA ON APPLICATION RELEVANT TO THE ACTIVE SUBSTANCE (ANNEX IIA 3.1 TO 3.6)

B.3.1.1 Function

Dichlobenil is a non-selective herbicide.

B.3.1.2 Effects on harmful organisms

B.3.2.1. Nature of the effects

The exerted effects are an inhibition of germination and actively growing meristems, primarily acting on growing points and root tips.

Dichlobenil can inhibit the incorporation of cellulose into cell walls (Kawamura et al., 1976; Hogetsu et al., 1974; Montezinos and Delmer, 1980; Meyer and Herth, 1978; Umetsu et al., 1976), however the exact mode of action is not yet known. Both mono- and dicotyledous plants are controlled, especially by inhibition of germinating seeds and growth of young seedling plants. Older plants, especially when shallow-rooted, are controlled under favourable conditions and/or with high dosages. The growth of sprouts of perennial weeds is stopped. Established plants tolerate Dichlobenil well.

B.3.2.2. Translocation (apoplastic, synplastic or both)

The fate of Dichlobenil has been studied most extensively with bean seedlings. Dichlobenil is absorbed by the roots and translocated throughout the plant. In the leaves two competitive processes, evaporation and degradation, take place.

Plants grown in soils treated with Dichlobenil are exposed to BAM also, and due to the transport of BAM with the transpiration stream, this compound and its hydroxyl-metabolites are the main sources of residues under practical conditions.

(Verloop, 1972; Beynon and Wright, 1972)

B.3.1.3 Field of use

Dichlobenil can be used for selective weed control of annual and perennial weeds, including light grass vegetation, vineyards, woody ornamentals, amenity plantings and forests. It can, furthermore, be applied as a total weed killer on industrial sites and other non-crop areas.

B.3.1.4 Harmful organisms controlled and crops or products protected or treated

B.3.1.4.1. Details of existing and intended uses

Dichlobenil is a broad-spectrum herbicide that can be used as a selective weed killer for use under most established trees and shrubs and on non-crop land for control of germinating seeds and existing

weeds.

B.3.1.4.2. Details of harmful organisms against which protection is afforded (to be provided if relevant)
In general it can be stated that most germinating seeds and seedlings from both annual and perennial weeds are susceptible to Dichlobenil.

B.3.1.4.3. Effects achieved (e.g sprout suppression, reduction stem length e.g. to be provided if relevant)

The effects that are achieved by the use of Casoron® G are the prevention of weed seed germination and seedling emergence. Its use also prevents weed growth in crop and non-crop areas following application, by inhibiting root growth. Dichlobenil also kills top growth. Although the primary point of action is the meristematic tissue (above and below the soil surface) it also kills the leaf tissue of existing weeds. Dichlobenil does not prevent the start of germination, as this is primarily cellular expansion, but once the cell is actively growing, Dichlobenil is taken into the plant and kills the areas of cell division. In seeds/seedlings, if they are in the treated band, the proportion of meristematic tissue compared to ordinary cells is much higher and the plants are rapidly killed.

B.3.1.5 Mode of action

B.3.1.5.1 Mode of action of the active substance (biochemical, physiological mechanisms)

Dichlobenil can inhibit biosynthesis of cellulose in plant cell walls. However, this does not necessarily mean that inhibition of cellulose biosynthesis is the single mode of action of Dichlobenil. The exact mode of action of Dichlobenil is not yet precisely known.

B.3.1.5.2 Details of active metabolites and/or degradation products if relevant – chemical properties (chemical name, EINECS/ELINCS number, CIPAC, molecular mass, structure, formula etc.)

Not applicable; Dichlobenil is the active substance. There are no metabolites or degradation products known which exert the herbicidal effect.

B.3.1.5.3 Available information relating to formation of active metabolites and/or degradation products (processes, mechanisms, reactions, kinetic data, environmental and other factors effecting the conversion etc.)

Not applicable; Dichlobenil is the active substance. There are no metabolites or degradation products known which exert the herbicidal effect.

B.3.1.6 Information on possible occurrence of resistance

Dichlobenil is an herbicide, which inhibits the incorporation of glucose into cellulose and prevents the

creation of new cell walls. It appears to have multi-site activity and although different weed species have different sensitivities to Dichlobenil, no known build-up of resistance has occurred during the 40 years it has been used.

Dichlobenil belongs to Group L, as defined by the Herbicide Resistance Action Committee (HRAC), which includes all active substances that cause inhibition of cell wall synthesis regardless of mode of action. Weed Science Society of America (WSSA) further divide this group according to mode of action.

B.3.2 Data on application relevant to the plant protection product (Annex IIIA 3)

B.3.2.1 Field of use

Casoron® G is proposed for use as herbicide for total weed control on non-crop land (e.g. industrial sites, roadsides, railway tracks, along fences) and as a selective herbicide in grapes.

B.3.2.2 Effects on harmful organisms

Casoron® G, a non-selective herbicide, is a powerful inhibitor of germinating seedlings and of actively growing meristems. Dichlobenil acts primarily on growing points and root tips.

B.3.2.3 Details of the intended use

In general it can be stated that most germinating seeds and seedlings from both annual and perennial weeds are susceptible to Dichlobenil.

B.3.2.4 Application rate

For grapes the application rate can range from 40 - 80 kg Casoron® G/ha (equal to 2.7 - 5.4 kg Dichlobenil/ha).

For Non-crop land the application rate can range from 30 - 80 kg Casoron® G/ha (equal to 2.03 - 5.4 kg Dichlobenil/ha).

B.3.2.5 Concentration of active substance in the material used

Casoron® G is a ready-to-use granular formulation that does not require dilution before use. The concentration of the active substance in the formulation is 67.5 g/kg.

B.3.2.6 Method of application

Casoron® G is either applied with manually operated granule spreaders, with motorised equipment (e.g. knapsack spreader) or with tractor-mounted equipment suitable for granular applications.

B.3.2.7 Number and timing of applications, duration of protection

For use in vines the general application time will be February-March; for non-crop uses this will be February-May, depending on the climatologically circumstances. One single treatment per year, up to

3 weeks before the leaf emergence is normally recommended, but also a split application (one half of the application rate in late autumn, the other in early spring) is possible.

B.3.2.8 Necessary waiting periods or other precautions against phytotoxic effects

Casoron® G is not recommended for use on areas where rotational crops can be planted. Re-planting of a treated area is not recommended for 6-12 months after last treatment. However, due to the properties of both parent (DT50 of 39 – 296 days) and the main metabolite BAM (DT50(extrapolated) of 404 – 2666 days), which is also the main metabolite in grapes, an accumulation of especially the metabolite in the ground after application in more than one growing season has to be considered and should be investigated. The outcome can influence the view on the waiting periods and/or the elaboration of the MRL.

Use of Casoron® G is not recommended within 6-12 months after planting (ornamental) shrubs and trees.

B.3.2.9 Proposed instructions for use

In general, application to a dry or slightly moist soil during cool weather conditions will give the best results, particularly if there is a likelihood of rain after application. Good results depend on careful application. The following points should be minded (based on draft label as submitted by the notifier):

- apply evenly
- apply only to established crops
- where mulching is practiced, apply before mulching
- ensure that granules do not fall or blow on other areas than intended
- prevent granules from lodging on crop leaves or in the leaf axils
- avoid local overdosing
- do not apply near hops and glasshouses
- do not apply to sites within 18 months of re-planting or sowing.

B.3.3 Summary of data on application

Relevant data for the application of the active substance (see B.3.1) and the plant protection product (see B.3.2) are available. However, the accumulation of especially the metabolite in the ground after application in more than one growing season has to be considered and should be investigated. The outcome can influence the view on the waiting periods and/or the elaboration of the MRL.

B.3.4 Further information on the active substance (Annex IIA 3.7 to 3.9)

B.3.4.1 Recommended methods and precautions concerning handling, storage, transport of fire

See safety data sheet as submitted by the notifier.

Handling: Do not get in eyes, on skin, on clothing. Avoid dispersion of dust in air. Do not eat, drink, smoke when handling.

Apply local exhaust ventilation at points of dust generation.

Storage: Store in a cool, dry place. Store in closed original drums

Fire-fighting measures: suitable are alcohol-type foam or universal-type foam, as well as for small fires: CO₂, dry chemical or water spray. Water jets are not suitable. Protective equipment to be used: body-covering protective clothing, full "turn-out" gear. Self-contained breathing apparatus.

B.3.4.2 Procedures for destruction or decontamination

B.3.4.2.1 Controlled incineration

The most appropriate method for safe disposal is controlled incineration according to EEC Directive 94/67 in a special incinerator for chemicals. Since Dichlobenil does not contain a halogen content >60%, the following criteria should be adhered to: temperature > 850°C, residence time at least two seconds and a presence of more than 6% oxygen.

The pyrolytic behaviour of Dichlobenil under controlled conditions at 800°C does not need to be assessed, as the molecule does not contain more than 60% halogens.

B.3.4.2.2 Others

No methods, other than controlled incineration, are recommended for safe disposal.

B.3.4.3 Emergency measures in the case of an accident

There are no well-defined methods available. Containment of the spillage followed by general decontamination methods for chemicals are proposed

B.3.5 Further information on the plant protection product (annex IIIA 4)

B.3.5.1 Packaging (type, material, size, compatibility)

B.3.5.1.1 Fully description

Casoron® G is commercial available in the EU in the following packaging:

1 kg shaker: The 1 kg shaker is a laminated cardboard can with steel bottom and plastic doses cap for manual application, height 250 mm, diameter 80 mm.

5 kg container: The 5 kg container is an HDPE container with tamper-evident screw cap to be used with a granule spreader, size (in mm): 205 x 115 x 315.

15 kg bag in box and 25 kg bag in box: The 15 and 25 kg box in bags are laminated bags glued in a cardboard box to be used for motorised (15 and 25 kg) and/or tractor-mounted (25 kg) equipment.

Sizes (in mm): 250 x 240 x 270 for 15 kg pack size and 250 x 240 x 410 for the 25 kg pack size.

(van Oevelen and Verhoeven, 2004)

B.3.5.1.2 Suitability (leakproofness, resistance to transport, and handling etc)

Casoron[®] G is not classified and is not regulated for Transport of Dangerous Goods: UN approved packaging is therefore not required (van Oevelen and Verhoeven, 2004).

B.3.5.1.3 Resistance of packaging material in accordance with GIFAP Monograph No. 17

After 6, 12, 24 and 36 months the state of the packaging remained unaffected by Casoron[®] G, and was only described as a little bit dusty. This was found shelf-life stability study (Poel, 2004) where samples from a production campaign of Casoron[®] G were included. During the study, the test sample was stored under ambient warehouse conditions. The state of the packaging (cardboard box, containing an aluminium lined paper bag) was inspected visually after 6, 12, 24 and 36 months storage under ambient warehouse conditions.

No further studies on the resistance of the other packaging materials have been performed. A corrosion characteristics test with the active substance revealed no indication of changes to various test materials and is summarized below. Furthermore the other formulation components do not possess properties that might affect the packaging material.

Dichlobenil is not corrosive in nature. This was found in a study of Poel and de Bree (1996), where the corrosion characteristics of Dichlobenil were investigated conform ASTM G31-72 for 28 weeks at 40°C. Specimen of carbon steel, stainless steel AISI 304, aluminum, polyethylene and polyethylene coated paper were used as test materials. The last three specimens were from standard Crompton Corporation packaging materials. Parameters investigated were weight change and appearance of the specimen.

B.3.5.2 Procedures for cleaning application equipment

The 1 kg shaker and 5 kg container are single-use and ready-to-use packagings. No cleaning procedures are therefore described, nor required, for these two packagings.

▪ Safety standards

The user is expected to have carried out a full risk assessment and have implemented local safety regulations (e.g. a COSHH assessment in the UK). Special attention should be paid to the following points:

Follow any specific decontamination procedures indicated in a product label.

Ensure that all decontamination equipment is stored in a safe location.

Ensure safe procedures are followed for the containment, storage and disposal of dilute wastes

Ensure proper storage of decontaminated PPE.

Ensure access to a supply of clean fresh water for emergency and handwashing uses.

- Principles:

The following principles minimize the potential risk during decontamination procedures:

-Decontaminate PPE immediately after use. Plan application to avoid surplus treatment or needless decontaminations (e.g. use herbicides after other products).

- Procedures:

Personal Protective Equipment

Impermeable overalls, boots and face shields should be washed and scrubbed clean in running water, dried and stored in an area free from contamination.

Permeable, (cotton-type re-usable) overalls should be laundered after use.

Launder protective clothing separately from normal clothing

Use a pre-wash treatment

Use a hot wash (60°C) wherever possible

Use 1.5 times the recommended amount of detergent

If heavily contaminated with pesticide concentrate the item should be disposed of as contaminated waste

Gloves should be washed prior to removal. Disposable gloves and coveralls should be removed after use and disposed of as contaminated waste.

Application equipment

As the equipment to be used is either ready-to-use or especially designated for this purpose, the only recommended procedure is to store in a properly designated store, away from sources of contamination.

- Effectiveness of decontamination procedure

Personal Protective Equipment

The primary exposure mechanism for most pesticides is dermal, and for that reason the appropriate selection, use and storage of personal protective clothing is paramount in minimising the users risks to health

A number of variables have been identified as affecting the outcome of the process. These include soil type, textile substrate characteristics and decontamination factors. An overview document (Laughlin, 1993 – this reference is not included in the dossier) draws together a large amount of research in the field and this has been used as a basis for the following overview on the procedures for PPE decontamination. This review of recent work on the mechanisms of soil removal from textiles assists in understanding decontamination of pesticide protective clothing. The review provides explanatory conclusions about residue retention as a basis of making recommendations for the most effective decontamination procedures. Some pesticides produce very idiosyncratic responses to decontamination, whilst others exhibit noticeable and unique responses to a highly alkaline medium, or to bleach, or are quickly volatilised. Responses such as these do not apply to other pesticides undergoing decontamination. Given this caution, there are soil, substrate, and

solvent responses that do maximise residue removal. Residue removal is less complete as the concentration of pesticide increases. The concentration of pesticide in fabric builds with successive exposures, and the more concentrated the pesticide, the more difficult the removal. Use a pre-wash product and/or pre-soak. The surfactant and/or solvent in a pre-wash product is a booster in residue removal. Residues transfer from contaminated clothing to other clothing during the washing cycle. Use a full washer of water for a limited number of garments to increase residue removal. A higher the washing temperature is better for decontamination of clothing. Generally, this means a water temperature of at least 40°C, and preferably 60°C. Select the detergent shown to be more effective for the formulation: heavy-duty liquid detergents for emulsifiable concentrate formulations and powdered phosphate detergents for wettable powder formulations. If the fabric has a soil-repellent finish, use 1.25 times the amount recommended on the detergent label. For water hardness above 300 ppm, an additional amount of powdered phosphate detergent is needed to obtain the same level of residue removal as obtained with the heavy-duty liquid detergent when laundering fabrics with the soil repellent finish. The mechanical action of agitation increases dislodgement of particulate material. Too many items in the washing apparatus or too low water volume, or both, decrease agitation and soil removal. Bleach can be used if desired. Fabric softener does not affect pesticide absorption or residue removal in laundering. Dry cleaning is not recommended because the solvents used in dry cleaning may be recycled through dilution, filtration, activated charcoal adsorption, or distillation. Pesticides still may be present in recycled solvents and can be transferred from one item to another, or from one load to subsequent loads of dry cleaning.

Spraying Equipment

No study has been carried out specifically to assess the effectiveness of the decontamination procedures recommended for Casoron® G. Granule spreading equipment will normally be used for application of Casoron® G only.

B.3.5.3 Re-entry period, waiting periods or other precautions to protect man, livestock and the environment

There are no pre-harvest intervals, re-entry intervals or withholding periods for Casoron® G envisioned or considered relevant following its proposed uses. However, as explained under B.3.2.8, an accumulation of especially the metabolite in the ground after application in more than one growing season has to be considered and should be investigated. The outcome can influence the view on the waiting periods and/or the elaboration of the MRL.

B.3.5.4 Recommended methods and precautions concerning handling, storage, transport or fire

Warehouse and user level storage

See Safety Data Sheet for Casoron® G. Standard measures include storage in a cool and dry place.

Transport

See Safety Data Sheet for Casoron® G. The product is not regulated by ADR, IMDG or ICAO.

B.3.5.5 Emergency measures in case of an accident

Fire

See Safety Data Sheet for Casoron® G. Standard measures include: extinguish with CO₂, dry powder, foam or water fog. Do not use water spray. Do not discharge extinguishing waters into streams, rivers and lakes. Firefighters should wear protective clothing, full "turn-out" gear. Self-contained breath apparatus.

Containment of spillages

See Safety Data Sheet for Casoron® G. In general, the product can be swept up and should be collected in a suitable container for disposal.

Protective clothing and equipment proposed

As the product is not classified as hazardous, no specific protective clothing and equipment is deemed necessary. The following recommendations are provided in the safety datasheet to minimize exposure to the product: in case of occurrence of dust respiratory protective equipment is required. Wear chemical resistant gloves. Use safety glasses with side shields. Wear protective clothing, such as long sleeves to minimize skin contact.

Characteristics: No specific requirements needed.

First aid measures

See See Safety Data Sheet for Casoron® G. The following measures are recommended:

- Swallowing

Do not induce vomiting. Rinse mouth with water. Obtain medical attention.

- Inhalation

Remove to fresh air. Obtain medical attention if symptoms persist.

- Skin contact

Wash skin with soap and water. No harmful effects expected

- Eye contact

Flush eyes thoroughly with water for several minutes. Obtain medical attention if discomfort persists.

B.3.5.6 Procedures for destruction or decontamination of the plant protection product and its packaging

No special procedures are deemed necessary, as the product is not classified.

B.3.5.6.1 Possibility of neutralization

There are no practical methods for chemical neutralization of the product. As the product is not classified, no procedures exist.

B. 3.5.6.2 Controlled incineration

Since dichlobenil and the formulation components in Casoron® G contain less than 60% chlorine, complete combustion will give CO₂, H₂O and N₂/N-oxides and possible some HCl. The formation of polyhalogenated-p-dioxines is unlikely. Conclusively, combustion is highly unlikely to give dangerous micro contaminants like polychlorinated dibenzodioxins and polychlorinated furans.

B. 3.5.6.3 Others

Not available.

B.3.6 References relied on

Section B.3 Data on application and further information (Annex IIA 3.1 - 3.9 and Annex IIIA 3 – 4.6)

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIA 3.2.1/01	Kawamura, H., Kamisaka, S., Masuda, Y.	1976	Regulation of lettuce hypocotyl elongation by gibberellic acid Plant And Cell Physiology 17:23-34 CA - 14 Non-GLP, Published	N	-
IIA 3.2.1/02	Hogetsu, T., Shibaoka, H., Shimokoriyama M.	1974	Involvement of cellulose synthesis in actions of gibberellin and kinetin on cell expansion 2,6-dichlorobenzonitril as a new cellulose-synthesis inhibitor Plant And Cell Physiology 15:389-393 CA - 26 Non-GLP, Published	N	-
IIA 3.2.1/03	Montezinos, D., Delmer, D.P.	1980	Characterization of inhibitors of cellulose synthesis in cotton fibers Planta 148: 305-311 CA - 27 Non-GLP, Published	N	-
IIA 3.2.1/04	Meyer, Y., Herth, W.	1978	Chemical inhibition of cell wall formation and cytokinesis, but not of nuclear division, in protoplasts of nicotiana tabacum L. cultivated in vitro Planta 142: 253-262 CA - 28 Non-GLP, Published	N	-
IIA 3.2.1/05	Umetsu, N., Satoh, S., Matsuda, K.	1976	Effects of 2,6-dichlorobenzonitrile on suspension-cultured soybean cells Plant And Cell Physiology 17:1071-1075 CA - 88 Non-GLP, Published	N	-
IIA 3.2.2/01	Verloop, A.	1972	Fate of the herbicide Dichlobenil in plants and soil in relation to its biological activity Residue Reviews 43:55-103 CA - 214 Non-GLP, Published	N	-

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIA 3.2.2/02	Beynon, K.I., Wright, A.N.	1972	The fates of the herbicides chlorthiamid and Dichlobenil in relation to residues in crops, soils and animals Residue Reviews 43:23-53 CA - 215 Non-GLP, Published	N	-
IIIA 4.1.1	van Oevelen, W.A.M. Verhoeven, L.C.	2004	Casoron G – description and specification of the packaging and materials used in packaging, size, capacity, size of the openings, types of closure and seals & suitability of the packaging and closures Crompton Europe BV, The Netherlands Report no. AM950/13/2004 Non-GLP, unpublished	Y	CHEM
IIIA 4.1.2	van Oevelen, W.A.M. Verhoeven, L.C.	2004	Casoron G – description and specification of the packaging and materials used in packaging, size, capacity, size of the openings, types of closure and seals & suitability of the packaging and closures Crompton Europe BV, The Netherlands Report no. AM950/13/2004 Non-GLP, unpublished	Y	CHEM
IIIA 4.1.3/01	Poel, E.N.	2004	A storage stability study of Casoron G; 3 years under warehouse conditions in original packaging Crompton Europe BV, The Netherlands Report no. 951/09/2003 GLP, unpublished	Y	CHEM
IIIA 4.1.3/02	Poel, E.N. de Bree, E.W.	1996	Corrosion characteristics of technical Dichlobenil Uniroyal Chemical BV, The Netherlands Report no. 56212/04/1995 GLP, unpublished	Y	CHEM

B.4 PROPOSALS FOR CLASSIFICATION AND LABELLING

B.4.1 PROPOSALS FOR THE CLASSIFICATION AND LABELLING OF THE ACTIVE SUBSTANCE (ANNEX IIA 10)

Physical and chemical properties

No classification and labelling is needed based on the physical and chemical properties of the active substance dichlobenil.

Human health effects

Justified proposals for classification and labelling of the active substance, relating to human health effects, according to Directive 2001/59/EC are listed below.

Hazard symbol	: Xn
Indication of danger	: harmful
Risk phrases	: R40 "Limited evidence of a carcinogenic effect", category 3
Safety phrases	: no obligatory safety phrases for professional use

Justification for the proposal:

R40: Obligatory for substances which cause concern for man owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment. There is some evidence from appropriate animal studies (110 week oral study in rat), but this is insufficient to place the substance in category 2.

Ecotoxicological effects

Classification is based on the following:

- Acute toxicity is the toxicity to fish, crustaceans (*Daphnia*/mysid shrimp), algae or higher aquatic plants.
- 96h-LC₅₀ fish is 7.2 mg a.s./L.
- 48h-EC₅₀ *Daphnia* is 6.2 mg a.s./L; 96h-LC₅₀ *Mysidopsis bahia*: 2.37 mg a.s./L.
- 72h-EC₅₀ algae is > 3.2 mg a.s./L.
- 14d-EC₅₀ *Lemna gibba* is 0.0279 mg a.s./L.
- The log P_{OW} value is 2.70.
- The test substance will not hydrolyse.
- The test substance is not readily biodegradable.
- The solubility in water is ca. 21 mg/L.

Based on this information the hazard classification of the active substance dichlobenil is N, R50/R53.

B.4.2 PROPOSALS FOR THE CLASSIFICATION AND LABELLING OF PREPARATIONS (ANNEX IIIA 12.3 AND 12.4)

Physical and chemical properties

No classification and labelling is needed based on the physical and chemical properties of Casoron® G.

Human health effects

Justified proposals for classification and labelling of the preparation Casoron® G, relating to human health effects, according to Directive 2001/59/EC are listed below.

Hazard symbol	:	Xn
Indications of danger	:	harmful
Risk phrases	:	R40 "Limited evidence of a carcinogenic effect", category 3
Safety phrases	:	no obligatory safety phrases for professional use

Justification for the proposal

R40: obligatory for formulations which contain substances classified with R40 at concentrations at or above the limit value of 1%. As dichlobenil is classified as carcinogenic and present at more than 1%, R40 is assigned to the preparation.

Ecotoxicological effects

Classification is based on the following:

- No aquatic toxicity studies with the formulation are available.
- The active substance has been assigned R50/53 based on its toxicity to *Lemna gibba* and its biodegradability characteristics.
- 14d-EC₅₀ *Lemna gibba* is 0.0279 mg a.s./L.
- The other components of Casoron G pose no environmental risks.
- Concentration of the active substance in the formulation is 6.75% w/w.
- According to Directive 2006/8/EG a substance with R50/53 and $0.01 \text{ mg/L} < \text{EC}_{50} \leq 0.1 \text{ mg/L}$ leads to R50/53 for a formulation when its concentration in this formulation is $\geq 2.5\% \text{ w/w}$.

Based on this information the hazard classification of the formulation Casoron G is N, R50/R53, S60, S61.

B.4.3 REFERENCES RELIED ON

The proposed classification and labelling for the active substance is based on the evaluation as presented in section B.2, B.6 and B.9.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

B.5 METHOD OF ANALYSIS

B.5.1 ANALYTICAL METHODS FOR FORMULATION ANALYSIS (ANNEX IIA 4.1; ANNEX IIIA 5.1)

B.5.1.1 Analytical method for technical active substance

I) Analytical method for the technical active substance – GC-FID

Characteristics of the study

Reference	: van Zeijl, 2003a	Test substance	: 2,6-Dichlorobenzonitrile techn.; batch no. AM2B19A063
Year of execution	: 2002/2003	Purity	: 99.2% w/w
Guideline	: SANCO/3030/99 rev. 4, 11/07/00		
GLP	: yes	Acceptabel	: yes

Study design

An analytical GC-method is described for the determination of 2,6-dichlorobenzonitrile in Dichlobenil technical (2,6-dichlorobenzonitrile technical; 2,6-DBN) by gas chromatography and internal standardization with 4-chlorobenzonitrile (method no. BAI 41 001).

The GC conditions were:

Detector:	Flame-ionisation detector (FID)
Column:	Fused silica capillary, 0.25 µm OV-17, 30 m x 0.32 mm (i.d.)
Temperature	Column: 130°C, injection: 300°C, detector: 250°C
Carrier gas:	Nitrogen, 80 mL/min

The samples of the technical active substance in combination with the internal standard 4-chlorobenzonitrile were dissolved in 50 mL acetone and an aliquote was directly applied to the GC. The specificity of the method was determined by GC-MS.

Results

The results are summarized in Table 5.1.1.

II) Analytical method for the technical active substance – CIPAC method

Handbook reference

Author	: Henriët et al., 1983
Method	: CIPAC method Dichlobenil 73

A CIPAC method is available for the determination of Dichlobenil technical (CIPAC method no. 73).

The method is based on the determination of Dichlobenil, dissolved in dichloroethane, by GC-FID using methyl myristate as internal standard.

According to the guideline no additional validation data are required for CIPAC methods since they are

collaboratively tested.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Table B.5.1.1: Method validation for 2,6 dichlorobenzonitrile in the technical active substance

Analyte	Interference/Specificity	Linearity range (% w/w) ¹⁾ [r]	Accuracy (% recovery)	Content (% w/w) ¹⁾	Precision – repeatability (% RSD) [n]	Reference/ Method no.
2,6 dichlorobenzonitrile (Dichlobenil, a.s.)	no interference/ specificity confirmed by GC-MS	40 – 160 [1.00]	99.7	100	0.135 [5x2]	Zeijl, E (2003a)/ BAI 41 001

1) % w/w as content of the active substance in the technical active substance

Summary, evaluation and assessment

Specificity, linearity, accuracy and precision of the method were determined for the active substance (technical grade). It has to be mentioned that the underlying data (concentration of the analyte and documentation, raw data of the measurement) for the determination of the accuracy are not available. Since according to the guideline, the accuracy does not have to be determined, this shortcoming is not considered as a relevant limitation. Furthermore, the precision was determined in 5 separate samples, analysed in duplicate. However, according to the guideline the precision has to be determined as 5 replicate sample determinations of one sample. Since the relative standard deviation did meet the criteria of the guideline it is considered acceptable.

Acceptability

The study is considered acceptable for the overall evaluation.

Conclusions

The described GC-FID method (method no. BAI 41 001) is validated for the determination of 2,6-dichlorobenzonitrile in Dichlobenil technical. Furthermore, a CIPAC method is available for the determination of Dichlobenil technical (CIPAC method Dichlobenil 73).

B.5.1.2 Analytical method for impurities

For the analytical method of the specified impurities: see Volume 4 Annex C.

B.5.1.3 Analytical method for plant protection product**I) Analytical method for the plant protection product-****Characteristics of the study**

Reference	: Brown, 2004	Test substance	: Casoron G, lot no. MI-0395
Year of execution	: 2004	Purity	: contains 6.56 % w/w Dichlobenil
Guideline	: SANCO/825/00 rev. 6, 20/06/00		
GLP	: yes	Acceptabel	: yes

Study design

An analytical GC-method is described for the determination of 2,6-dichlorobenzonitrile in formulated material (Casoron G) by gas chromatography and internal standardization with 4-chlorobenzonitrile (method no. GRL-GM-1117). The samples of the technical active substance in combination with the internal standard 4-chlorobenzonitrile were dissolved in acetone and an aliquote was directly applied to the GC-FID.

The GC conditions were:

Detector:	Flame-ionisation detector (FID)
Column:	DB-17, 30m x 0.53 mm (i.d.)
Temperature	Column: 250°C, injection: 250°C, detector: 300°C
Carrier gas:	Helium, 40 mL/min

The specificity of the method was determined by GC-MS.

Results

The results are summarized in Table 5.1.3.

II) Analytical method for the plant protection product – CIPAC method**Handbook reference**

Author	: Henriët et al., 1983
Method	: CIPAC method Dichlobenil 73

A CIPAC method is available for the determination of Dichlobenil in two different formulation types: next to wettable powders and also in granules, which is the formulation type of the indented use. This method is based on the extraction with dichloroethane and determination of Dichlobenil by GC-FID using methyl myristate as internal standard.

According to the guideline no additional validation data are required for CIPAC methods since they are collaboratively tested.

Table B.5.1.3: Method validation for 2,6 dichlorobenzonitrile in the plant protection product

Analyte	Interference/Specificity	Linearity range (mg) [r]	Accuracy (% recovery)	Content (mg) ¹⁾	Precision – repeatability (% RSD) [n]	Reference/ Method no.
2,6 dichlorobenzonitrile	No interference, specificity not determined	20 – 81 [1.00]	99.5	50	0.8 [5x2]	Brown, 2004 GRL-GM-117

Summary, evaluation and assessment

Interference, linearity, accuracy and precision of the method were determined for the active substance in the formulated product.

The precision was determined in 5 separate samples, analysed in duplicate. However, according to the guideline the precision has to be determined as 5 replicate. Since the relative standard deviation did meet the criteria of the guideline it is considered acceptable. Chromatographs generated from the analysis of Dichlobenil Standard solution, Dichlobenil Technical solution, Casoron G Sample solution and Casoron G Placebo Sample solution by method GRL-GM-117 confirm specificity (no interference) of the method [Tutty and Riggs, 2006].

Acceptability

The study is considered acceptable for the overall evaluation.

Conclusions

A CIPAC method is available for the determination of granular Dichlobenil technical (CIPAC method Dichlobenil 73), based on the extraction with dichloroethane and determination of Dichlobenil by GC-FID using methyl myristate as internal standard.

The described GC-FID method (method no. GRL-GM-117) is validated for the determination of 2,6-dichlorobenzonitrile in formulated material (Casoron G).

B.5.2 ANALYTICAL METHODS (RESIDUE) FOR PLANTS, PLANT PRODUCTS, FOODSTUFFS OF PLANT AND ANIMAL ORIGIN, FEEDINGSTUFFS (ANNEX IIA 4.2.1; ANNEX IIIA 5.2)

B.5.2.1 Analytical method for plants and plant products

The residue definition in plant (products) comprises only 2, 6-dichlorobenzamide (BAM), the main metabolite of the parent compound Dichlobenil.

I) Applicability of a multi-residue methods (MRM)

In total three reports are submitted addressing the applicability of the following multi-residue method:

- a) FDA method for the determination of 2,6-dichlorobenzamide in apples and hazelnut (Pouwelse and van Loo, 1992),
- b) DFG method S 19 for the determination of 2,6-dichlorobenzamide in grape (Specht, 1991a),
- c) DFG method S 19 for the determination of 2,6-dichlorobenzamide in apple (Specht, 1991b).

Following the decision tree for MRM testing of the FDA, Pouwelse and van Loo (1992) did show that no MRM was applicable for the determination of 2,6-dichlorobenzamide in apples and hazelnut, since none of the prescribed clean-up methods was appropriate. Grapes were not investigated in this study.

Specht (1991a and 1991b; in German) showed that DFG method S 19 is applicable for the determination of 2,6-dichlorobenzamide in grape and apple.

Results

The results are summarized in Table B.5.2.

Acceptability

The method is not considered as suitable for the overall assessment as no ILV is submitted.

II) Handbook reference

General method description – metabolite 2,6-dichlorobenzamide (BAM) in crops, wine, water, soil and hydrosol

Author	: van Rossum et al., 1978
Method description	: Determination of Dichlobenil and its metabolite 2,6-dichlorobenzamide (BAM)

A handbook monograph on Dichlobenil is submitted, including a method description for the residue analysis. For Dichlobenil a method based on either steam distillation or column chromatography and GC-ECD is mentioned but no further information is provided. Furthermore, methods recommended for the determination of 2,6-dichlorobenzamide (BAM) in crops, wine, water, soil and hydrosol are

described.

The methods comprise the following steps:

- extraction of the sample (different extraction solutions, depending on the matrix),
- clean-up by column chromatography on alumina,
- detection by GC-ECD.

The conditions for the analysis by GC-ECD were:

Detector:	Electron capture detector (ECD)
Column:	Chromosorb W HP, 80-100 mesh, coated with 5% SE 30 (Dichlobenil) or 2% XE-60 (BAM), 3 mm (i.d.) x 100 cm (Dichlobenil) or 120 cm (BAM)
Temperature	Column: 130°C, injection: 200°C, detector: 190°C (Dichlobenil) or Column: 185°C, injection: 200°C, detector: 200°C (BAM)
Carrier gas:	Nitrogen, 50 mL/min

The reference does not include any method validation data. The selectivity of the method is not confirmed. Recovery and sensitivity limit are mentioned, but the underlying data are not available. Therefore the report is not considered as suitable for the overall assessment, could not be summarized in Table B.5.2 and no LOQ could be derived.

III) Analytical method for plant (products) – BAM, apples and grapes, GC-ECD

Characteristics

Reference	: van Balkom, 1993	Test substance	: 2,6 dichlorobenzamide, batch no. ARS81C25N
Year of execution	: 1992 - 1993	Purity	: > 99.5%
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Acceptable	: no
GLP	: yes		

Study design

An analytical method based on gas chromatography with electron capture detection (GC-ECD) is described for the determination of 2,6-dichlorobenzamide (BAM) in apples and grapes (without stalks).

The method comprises the following steps:

- extraction of the homogenised samples (grinded with anhydrous Na₂SO₄) with ethylacetate,
- clean-up by column chromatography on alumina (6 cm activated Al₂O₃, eluent: ethanol/petroleum ether),
- measurement of diluted samples, applying GC-ECD.

The conditions for the analysis by GC-ECD were:

Detector:	Electron capture detector (ECD)
Column:	Chromosorb W HP, 80-100 mesh, coated with 2% silicone OV-225, 100 cm x 3 mm (i.d.)
Temperature	Column: 235°C, injection: 250°C, detector: 300°C
Carrier gas:	Nitrogen (flow rate not determined)

Results

The results are summarized in Table B.5.2.

Acceptability

The study is not considered acceptable for the overall evaluation, since the set-up of the study does not fulfil the criteria for a correct method validation as defined in the guideline. Main shortcoming is the amount of measurements per fortification level ($n = 2$). The method specificity is not addressed and confirmed. The lowest fortification level (0.5 mg/kg) is too high for the required purposes as concentrations of at least 0.1 mg/kg BAM should be measurable. Therefore, no LOQ could be derived.

IV) Analytical method for plant (products) – Dichlobenil and BAM, grapes, GC-ECD

Characteristics

Reference	: Brereton, 2000 (Appendix F)	Test substances	: Dichlobenil, batch no. ARS-9108BA
Year of execution	: n.i.		: 2,6-dichlorobenzamide (BAM), batch no. ARS-81C25N
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Purity	: Dichlobenil: 100%
GLP	: no (not signed appendix of the study report)	Acceptable	: 2,6-dichlorobenzamide: 99.7%
			: no

Study design

An analytical method (Agrisearch method Dichlobenil-BAM/Crops/DB/99/1, based on Meth-83 4/96 and Meth-84 4/96) is described for the determination of Dichlobenil and its metabolite 2,6-dichlorobenzamide (BAM) in grapes.

The method comprises the following steps:

- extraction of the homogenised samples (stalks removed) with ethyl acetate (for determination of BAM) or with 20% ethyl acetate in hexane (for determination of Dichlobenil),
- clean-up of the extract applying gel permeation chromatography,
- measurement, applying GC-ECD.

The GC conditions were:

Detector:	Electron capture detector (ECD)
Column:	For determination of Dichlobenil: fused silica capillary, coated with DB17 (0.3 µm), 0.18 mm i.d. x 10 m For determination of BAM: fused silica capillary, coated with DB608 (0.5 µm), 30 m x 0.32 mm (i.d.)
Temperature	For determination of Dichlobenil: Injection = 300°C, oven = 280°C, detector = 300°C For determination of BAM: Injection = 250°C, oven = 280°C, detector = 310°C
Carrier gas:	nitrogen, 40 mL/min

Results

The results are summarized in Table B.5.2.

Acceptability

The study is not considered acceptable for the overall evaluation, since the set-up of the study does not fulfil the criteria for a correct method validation as defined in the guideline. Main shortcoming is the amount of measurements per fortification level ($n = 2$). Furthermore, the method specificity is not addressed and confirmed. Only recovery data were reported without the supporting raw data.

Therefore it is not possible to determine if the recovery values are corrected for control values or not. Furthermore, the chromatographs show that especially for Dichlobenil an unspecified component in the untreated samples blank co-eluting most likely with the analyte. Therefore, no LOQ could be derived.

V) Analytical method for plant (products) – Dichlobenil and BAM, grapes and processed fractions, GC-ECD

Characteristics

Reference	: Maselli, 1998 (Appendix VI)	Test substances	: Dichlobenil, batch no. AC-1366-124
Year of execution	: 1996-1998		: 2,6-dichlorobenzamide (BAM), batch no. ARS81C25N
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Purity	: Dichlobenil: 99.6%
			: 2,6-dichlorobenzamide: 99.5%
GLP	: yes	Acceptable	: no

Study design

The notifier additionally submitted the information on the method validation of the processing study (Maselli, 1998). In that study it is referred to various protocols, submitted as appendix to the report:

- Determination of Dichlobenil in cherries and modified for raisins (Morse Laboratories, INC. SOP# Meth-83): extraction with ethyl acetate in hexane, clean-up applying alumina column, measurement by GC-ECD;
- Determination of 2,6-dichlorobenzamide in cherries and modified for raisins and fruit juices (Morse Laboratories, INC. SOP# Meth-83): extraction with ethyl acetate, clean-up applying alumina column, measurement by GC-ECD,

In both protocols only typical GC conditions are listed with the remark that specific conditions will be noted on the individual chromatogram.

Results

Validation data are submitted for both Dichlobenil and BAM in grapes, raisins, grape juice.

In Table B.5.2 are only the relevant results (Dichlobenil and BAM in grapes) will be listed.

Acceptability

The study is not considered acceptable for the overall evaluation. The accompanying information is too less specific and too limited: In both protocols it is stated that only typical GC conditions are listed

with the remark that specific conditions will be noted on the individual chromatogram, which is not the case - the specific GC-ECD conditions are not described, the specificity of the method is not addressed and confirmed. The calibration curve is prepared with 4 instead of 5 determinations as requested in the guideline. Therefore, no LOQ could be derived.

VI) Analytical method for plant (products) – Dichlobenil and BAM, grapes, GC-ECD and GC-MS/MS

Characteristics

Reference	: Bacher, 2005	Test substance	: Dichlobenil, batch no. ARS-9108BA
Year of execution	: 2005		: 2,6-dichlorobenzamide (BAM), batch no. ARS-81C25N
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Purity	: Dichlobenil: 100%
GLP	: yes	Acceptable	: 2,6-dichlorobenzamide: 100%
			yes

Study design

An analytical method based on gas chromatography with electron capture detection (GC-ECD) is described for the determination of Dichlobenil and 2,6-dichlorobenzamide (BAM) in grapes. The sample preparation method for the determination of Dichlobenil comprises the following steps:

- extraction of the homogenised samples with ethyl acetate in hexane
- purification by alumina column clean-up, elution with 2% acetone in hexane
- analysis of concentrated and volume-adjusted samples, applying GC-ECD and GC-MS/MS.

The sample preparation method for the determination of BAM comprises the following steps:

- extraction of the homogenised samples with ethyl acetate, sodium sulphate
- after filtration and concentration of the extract dilution in 10% acetone in petroleum ether
- purification by alumina column clean-up, elution with 15% ethanol in petroleum ether
- analysis of concentrated and volume-adjusted samples, applying GC-ECD and GC-MS/MS.

The conditions for the analysis by GC-ECD were:

Detector:	Electron capture detector (ECD)
Column:	Varian SP Sil 24 CB (50% phenyl-and 50% dimethylpolysiloxane), 0.25 µm, 30 m x 0.32 mm (i.d.)
Temperature	Column: 60 - 270°C (Dichlobenil) or 80 – 270°C (BAM), injection: 230°C, detector: 300°C
Carrier gas:	Helium (10psi)

The conditions for the analysis by GC-MS/MS were:

Column:	Varian VF-17 ms 24 CB (50% phenyl-and 50% dimethylpolysiloxane), 0.25 µm, 30 m x 0.32 mm (i.d.)
Carrier gas:	Helium (10 psi)
Temperature	Column: 60 - 270°C (Dichlobenil) or 80 – 340°C (BAM), injection: 230°C, detector: 300°C
Fragments:	m/z 171 (confirmation); m/z 136 (quantitation) for Dichlobenil m/z 173 (confirmation) ; m/z 145 (quantitation) for BAM

Results

The results are summarized in Table B.5.2.

Acceptability

The study is considered acceptable for the overall evaluation. Eventhough the calibration curves do not in all cases completely cover the range as requested in the guideline (nominal concentration of the analyte $\pm$ at least 20%), LOQ were derived since based on the available data (measured ranges and the resulting high correlation factors) it can be assumed that all measurements were performed in the linear range.

VII) Independent Laboratory Validation: Analytical method for plant (products) – Dichlobenil and BAM, grapes, GC-ECD and GC-MS/MS

Characteristics

Reference	: Wolf, 2006	Test substance	: Dichlobenil, batch no. ARS-9108BA-A
Year of execution	: 2006		: 2,6-dichlorobenzamide (BAM), batch no. FUN81G02C
Guideline	: SANCO/825/00 rev.7, 17/03/04	Purity	: Dichlobenil: 100%
GLP	: yes	Acceptable	: 2,6-dichlorobenzamide: 99.9%
			yes

Study design

This study is an ILV of Bacher, 2005. Procedures for sample preparation and analysis are therefore equal.

The conditions for the analysis by GC-ECD were:

Detector:	Electron capture detector (ECD)
Column:	DP17 (30 m x 0.32 mm x 0.25 μ m Film); Agilent
Temperature	Column: 60 - 270°C (Dichlobenil) or 80 – 230°C (BAM), injection: 230°C, detector: 300°C
Carrier gas:	Helium (70 Kpa, constant flow)

The conditions for the analysis by GC-MS/MS were:

Column:	DP17 (30 m x 0.32 mm x 0.25 μ m Film); Agilent
Carrier gas:	Helium (6 psi/min, constant pressure)
Temperature	Column: 80 - 390°C (Dichlobenil) or 80 – 300°C (BAM), injection: 230°C, detector: 300°C
Fragments:	m/z 171 (confirmation); m/z 100 and 136 (quantitation) for Dichlobenil m/z 173 (confirmation); m/z 145 and 189 (quantitation) for BAM

Results

The results are summarized in Table B.5.2.

Acceptability

The study is considered acceptable for the overall evaluation.

B.5.2.2 Analytical method for products of animal origin

The notifier submitted no analytical method(s) for products of animal origin.

Based on the current intended use of Dichlobenil in grapes relevant intake levels (>0.1 mg/kg dry feed) of the metabolite BAM, the component of the residue definition, occur for cattle (see B.15.1).

Depending on the outcome of the requested data on animal metabolism for ruminants (see B.7.2) analytical methods for products of animal origin could be required in case the metabolism data indicate that significant residues (≥ 0.01 mg/kg) may occur in any edible part of the animal after intake of the residue levels in potential feedingstuffs at the 1x dose rate, a feeding study with BAM in ruminants will be required as well and validated analytical methods must be available for the determination of the relevant residues in the relevant animal matrices.

Table B.5.2: Summary of method validation of the analysis of Dichlobenil and its metabolite 2,6-dichlorobenzamide in apples and grapes

Matrix	Analyte	Dissolution/ extraction	Partition/clean-up	Quantification	Recovery fortification level (mg/kg) [n]	Recovery range (%) [overall mean]	Recovery (%)	Repeatability RSD (%)	LOQ (mg/kg)	Linearity (r ²) [range]	Reference; Remark
grapes	BAM	Acetone/water	gel permeation chromatography	GC-ECD	0.01 [2] 2.0 [2]	68-76 87-94 [81]	[72] [90]	n.a. n.a.	not derived	n.i.	Specht, 1991a (MRM, no ILV)
apples	BAM	Acetone/water	gel permeation chromatography	GC-ECD	0.01 [2] 0.5 [2]	103-109 103-104 [105]	[106] [104]	n.a. n.a.	not derived	n.i.	Specht, 1991b (MRM, no ILV)
apples	BAM	ethyl acetate	column chromatography (Al ₂ O ₃)	GC-ECD	0.5 [2] 2.6 [2]	105, 107 99, 100 [103]	106 99	n.a. n.a.	not derived	0.9994 [0.001 – 0.1 µg/mL]	van Balkom, 1993 (insufficient amount of data points; specificity not confirmed)
grapes	BAM	ethyl acetate	column chromatography (Al ₂ O ₃)	GC-ECD	0.5 [2] 2.6 [2]	92, 94 92, 97 [94]	93 95	n.a. n.a.	not derived	0.9994 [0.001 – 0.1 µg/mL]	van Balkom, 1993 (insufficient amount of data points; specificity not confirmed)
grapes	Dichlobenil	20% ethyl acetate in hexane	gel permeation chromatography	GC-ECD	0.02 [2] 0.05 [2] 0.10 [2]	103, 102 82, 87 76, 80 [88]	101 85 78	n.a. n.a. n.a.	not derived	n.i. ¹⁾ [0.0025 – 0.2 µg/mL]	Brereton, 2000 (insufficient amount of data points; specificity not confirmed)
grapes	BAM	ethyl acetate	gel permeation chromatography	GC-ECD	0.003 [2] 0.01 [2] 0.10 [2]	73, 72 71, 71 79, 80 [74]	73 71 80	n.a. n.a. n.a.	not derived	n.i. ¹⁾ [0.005 – 0.5 µg/mL]	Brereton, 2000 (insufficient amount of data points; specificity not confirmed)
grapes	Dichlobenil	20% ethyl acetate in hexane	column chromatography (Al ₂ O ₃)	GC-ECD	0.02 [6] 0.1 [6] 0.2 [6]	70 -90 85 – 93 80 – 97 [n.i.]	83 89 89	10 3.9 8.3	not derived	0.9994 [0.001-0.014 µg/mL]	Maselli, 1998 (too less calibration points, conditions not mentioned, specificity not confirmed)

Matrix	Analyte	Dissolution/ extraction	Partition/clean-up	Quantification	Recovery fortification level (mg/kg) [n]	Recovery range (%) [overall mean]	Recovery (%)	Repeatability RSD (%)	LOQ (mg/kg)	Linearity (r ²) [range]	Reference; Remark
grapes	BAM	ethyl acetate	column chromatography (Al ₂ O ₃)	GC-ECD	0.003 [6] 0.03 [6] 0.3 [6]	89 – 118 87 -102 91 -99 [n.i.]	104 96 95	9.6 5.4 3.6	not derived	0.9999 [0.01-0.14 µg/mL]	confirmed) Maselli, 1998 (too less calibration points, conditions not mentioned, specificity not confirmed)

grapes	Dichlobenil	ethyl acetate in hexane	column chromatography (Al ₂ O ₃)	GC-ECD	0.01 [5] 0.10 [5]	89 - 109 82 – 98 [95]	100 89	8 6	0.01	0.9831 [1.0-50 ng/mL]	Bacher, 2005
grapes	BAM	ethyl acetate	column chromatography (Al ₂ O ₃)	GC-ECD	0.01 [5] 0.10 [5]	103 – 109 95 – 105 [104]	106 102	2 4	0.01	0.9786 [1.0-75 ng/mL]	Bacher, 2005
grapes	Dichlobenil	ethyl acetate in hexane	column chromatography (Al ₂ O ₃)	GC-MS/MS	0.01 [5] 0.10 [5]	86 – 110 82 – 102 [94]	97 91	9 9	0.01	0.9998 [0.5-50 ng/mL]	Bacher, 2005
grapes	BAM	ethyl acetate	column chromatography (Al ₂ O ₃)	GC-MS/MS	0.01 [5] 0.10 [5]	106 – 111 91 – 104 [103]	108 98	2 5	0.01	0.9954 [1.0-100 ng/mL]	Bacher, 2005
grapes	Dichlobenil	ethyl acetate in hexane	column chromatography (Al ₂ O ₃)	GC-ECD	0.01 [5] 0.10 [5]	84-97 73-86 [84]	88 80	6 6	0.01	0.9993 0.5-100 ng/mL (ILV)	Wolf, 2006 (ILV)
grapes	BAM	ethyl acetate	column chromatography (Al ₂ O ₃)	GC-ECD	0.01 [5] 0.10 [5]	78-88 79-103 [88]	84 92	5 11	0.01	0.9915 2-100 ng/mL (ILV)	Wolf, 2006 (ILV)

Matrix	Analyte	Dissolution/ extraction	Partition/clean-up	Quantification	Recovery fortification level (mg/kg) [n]	Recovery range (%) [overall mean]	Recovery (%)	Repeatability RSD (%)	LOQ (mg/kg)	Linearity (r^2) [range]	Reference; Remark
grapes	Dichlobenil	ethyl acetate in hexane	column chromatography (Al ₂ O ₃)	GC-MS/MS	0.01 [5] 0.10 [5]	78-90 74-85 81	83 79	5 5	0.01	0.9987 0.5-100 ng/mL	Wolf, 2006 (ILV)
grapes	BAM	ethyl acetate	column chromatography (Al ₂ O ₃)	GC-MS/MS	0.01 [5] 0.10 [5]	85-109 94-98 [98]	102 95	9 2	0.01	0.9989 2-100 ng/mL	Wolf, 2006 (ILV)

n.a not applicable
n.i not indicated

1) Per analyte an example of a typical calibration curve is given. However since no underlying data are submitted it can not be assessed if the correlation coefficient is sufficient and acceptable.

WARNING: This document is an Evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

B.5.3 ANALYTICAL METHODS (RESIDUE) SOIL, WATER, AIR (ANNEX IIA 4.2.2 TO 4.2.4; ANNEX IIIA 5.2)

B.5.3.1 Analytical method for residues in soil

The residue definition in soil comprises the parent compound Dichlobenil and its metabolite 2,6-dichlorobenzamide (BAM).

Characteristics

Reference	: Bacher, 2002a	Test substance	: Dichlobenil, batch no. ARS-9108-BA
Year of execution	: 2002		: 2,6-dichlorobenzamide (BAM), batch no. ARS-81C25N
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Purity	: Dichlobenil: 100%
GLP	: yes	Acceptable	: 2,6-dichlorobenzamide: 100%
			yes

Study design

An analytical method based on gas chromatography with electron capture detection (GC-ECD) is described for the determination of Dichlobenil and 2,6-dichlorobenzamide in soil (loamy sand, LUFA Speyer standard soil 2.2.). The method comprises the following steps:

- extraction of the homogenised samples with 0.2% NH₄Cl aqueous solution/acetone/petroleum ether (17/75/75, v/v/v)
- partitioning of Dichlobenil into petroleum ether
- partitioning of BAM into ethyl acetate and
- purification on alumina cartridges
- measurement of diluted samples, applying GC-ECD.

The conditions for the analysis by GC-ECD were:

Detector:	Electron capture detector (ECD)
Column:	Chrompack CP Sil 8 CB Low Bleed fused silica, 0.25 µm, 30 m x 0.32 mm (i.d.)
Temperature	Column: 70 - 270°C, injection: 230°C, detector: 180°C (Dichlobenil) or 230°C (BAM)
Carrier gas:	Helium (flow rate not indicated)

As confirmatory method GC-MS as well as GC-MS/MS (only for Dichlobenil) were applied.

The analysis was performed under the following conditions:

Column:	Chrompack CP Sil 8 CB Low Bleed fused silica, 0.25 µm, 30 m x 0.32 mm (i.d.)
Carrier gas:	Helium (flow rate not indicated)
Temperature	Column: 70 - 270°C, injection: 230°C, detector: 140°C (Dichlobenil) or 183°C (BAM)
Fragments:	m/z 171 (quantitation); m/z 173 (confirmation) (MS) and m/z 171 → 136 confirmation for Dichlobenil (MS/MS)

m/z 173 (quantitation); m/z 175, 189 (confirmation) for BAM

Results

The results are summarized in Table B.5.3.

Acceptability

Even though for the repeatability of the determination of BAM at both levels only 4 measurements are available (in both cases one outlier was defined) is the study, based on the properties of the other determinations (recovery ranges and repeatability for Dichlobenil do all meet the requirement of the guidelines) considered acceptable for the overall evaluation.

B.5.3.2 Analytical method for residues in water

The residue definition in water comprises the parent compound Dichlobenil and its metabolite 2,6-dichlorobenzamide (BAM).

I) Analytical method for residues in water– Dichlobenil and BAM, surface water, GC-MS

Characteristics

Reference	: Carter, 2000	Test substance	: Dichlobenil, batch no. ARS-9108BA
Year of execution	: 1999/2000		: 2,6-dichlorobenzamide (BAM), batch no. ARS81C25N
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Purity	: Dichlobenil: 100%
GLP	: yes	Acceptabel	: 2,6-dichlorobenzamide: 99.7%
			yes

Study design

A solid phase extraction procedure with GC-MS described for the determination of Dichlobenil and BAM in using 2,4,6-trichlorobenzonitrile as internal standard. According to the author the method is expected to be applicable in drinking water, surface water and ground water, however, the validation is only performed in surface water.

The method comprises the following steps:

- extraction of sample material (1 L) on a divinylbenzene disk (Speeddisk™)
- elution with methylene chloride, concentrated under nitrogen using 1-heptanol as keeper due to volatility of Dichlobenil
- analysis of an aliquot by GC-MS.

The analysis was performed under the following conditions:

Column:	RTX-200, 0.5 µm film, 0.25 mm x 30 m
Temperature	Column: 270°C, injection: 250°C, detector: 280°C
Carrier gas:	Helium (flow rate not determined)
MS interface:	not indicated
Fragments:	m/z 171 (quantitation); m/z 173 (confirmation) for Dichlobenil
	m/z 173 (quantitation); m/z 175, 189 (confirmation) for BAM

Results

The results are summarized in Table B.5.3.

Acceptability

The study is considered acceptable for the overall evaluation.

II) Analytical method for residues in water– Dichlobenil, groundwater, HPLC-UV

Characteristics

Reference	: Kendall and Nixon, 2003	Test substance	: Dichlobenil, batch no. WO42763011V010
Year of execution	: 2003	Purity	: 99.3%
Guideline	: SANCO/825/00 rev. 6, 20/06/00		
GLP	: yes	Acceptable	no

Study design

A HPLC-UV method is described for the determination of Dichlobenil in groundwater using 2,4,6-trichlorobenzonitrile as internal standard. The method consists of the direct analysis of filtered aqueous samples using HPLC-UV:

The analysis was performed under the following conditions:

Detector:	UV, wavelength 220 nm
Column:	YMC Pack ODS AM (150 mm x 4.6 mm, 3 mm particle size)
Mobile phase:	0.1% H ₃ PO ₄ /CH ₃ CN (gradient).

Results

The results are summarized in Table B.5.3.

Acceptability

The study is considered acceptable for the overall evaluation.

III) Analytical method for residues in water– Dichlobenil, groundwater, GC-MS

Characteristics

Reference	: Wyma-Teitsma, 2003	Test substance	: Dichlobenil, batch no. ARS-9108-BA
Year of execution	: 2002 - 2003	Purity	: 100%
Guideline	: SANCO/825/00 rev. 6, 20/06/00		
GLP	: yes	Acceptable	no

Study design

A solid phase extraction procedure with GC-MS described for the determination of Dichlobenil in groundwater, using hexachlorobenzene as internal standard.

The method comprises the following steps:

- extraction of sample material on a divinylbenzene (DVB) speedisk
- elution with ethyl acetate
- analysis of an aliquot by GC-MS.

The analysis was performed under the following conditions:

Column:	HP-5 MS, 0.25 µm film, 30 m x 0.25 mm (i.d.)
Temperature	Column: 280°C, injection: 300°C, detector: 290°C
Carrier gas:	Not indicated
Fragments:	m/z 171 (most specific and sensitive for quantification), m/z 173 and m/z 136.

Results

The results are summarized in Table B.5.3.

The groundwater sample from one site (Lunschoten) did contain interfering substances at the retention time of Dichlobenil, accounting for 0.009 – 0.024 µg/L. Matrix-matched standards and fortified samples were corrected for this. In order to confirm that this effect was not due to the (un)specificity of the method but due to properties of the blank sample, an extra set of samples (MilliQ and groundwater from a different site – Drenthe) were analysed. Both, the MilliQ and the groundwater from the second site, did not contain an interfering peak (no dichlobenil). Therefore it seems most likely that the occurring irregularities were sample-specific matrix effects.

Acceptability

Since the recovery rate at the lower fortification level (0.05 µg/L) is not within the range of 70 -110% as requested in the guideline, the study is not considered acceptable for the overall evaluation.

IV) Analytical method for residues in water– Dichlobenil and BAM, groundwater, GC-MS

Characteristics

Reference	: Yu, 2004	Test substance	: Dichlobenil, batch no. 266-51B
Year of execution	: 2004		: 2,6-dichlorobenzamide (BAM), batch no. ARS81C25N
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Purity	: Dichlobenil: 99.5% 2,6-dichlorobenzamide: 100%
GLP	: yes	Acceptable	: yes

Study design

A solid phase extraction procedure (method GRL-GM-1197) with GC-MS described for the determination of Dichlobenil and BAM in using 2,4,6-trichlorobenzonitrile and as internal standard (2,4-BAM was in the first place used as internal standard for BAM, but appeared later to be not useful and suitable).

The method comprises the following steps:

- extraction of sample material (1 L) on a divinylbenzene (DVB) disk (Speeddisk™)
- elution with dichloromethane, using 1-heptanol as keeper
- analysis of an aliquot by GC-MS.

The analysis was performed under the following conditions:

Column:	HP-50+, 0.25 µm film, 30 m x 0.25 mm (i.d.)
Temperature	Column: 250°C, injection: 253°C, detector: 230°C
Carrier gas:	Helium, 1.0 mL/min
MS interface:	Not indicated

Fragments: m/z 171 (quantitation); m/z 136 (confirmation) for Dichlobenil
m/z 189 (quantitation); m/z 173 (confirmation) for BAM

Results

The results are summarized in Table B.5.3.

Acceptability

The study is considered acceptable for the overall evaluation.

V) Analytical method for residues in water– Dichlobenil and BAM, surface water, GC-MS, ILV

Characteristics

Reference	: Noon, 2001	Test substance	: Dichlobenil, batch no. ARS-9108-BA
Year of execution	: 2001		: 2,6-dichlorobenzamide (BAM), batch no. ARS81C25N
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Purity	Dichlobenil: 100%
GLP	: yes	Acceptable	2,6-dichlorobenzamide: 100%
			yes

Study design

An Independent Laboratory Validation (ILV) is performed of a GC-MS method (Analytical method No. AC—7005, Uniroyal study number 99055) for the determination of Dichlobenil and 2,6-dichlorobenzamide (BAM) in surface water, using 2,4,6-trichlorobenzonitrile as internal standard.

The method comprises the following steps:

- solid phase extraction of sample material (1 L) on a divinylbenzene disk (Speeddisk™)
- elution with methylene chloride, using 1-heptanol as keeper due to volatility of Dichlobenil
- analysis of an aliquot by GC-MS.

The analysis was performed under the following conditions:

Column: HP-5MS, 0.25 µm film, 30 m x 0.25 mm (i.d.)
 Temperature: Column: 280°C, injection: 250°C, detector: 280°C
 Carrier gas: Not indicated
 MS interface: Not indicated
 Fragments: m/z 171 (quantitation); m/z 173 (confirmation) for Dichlobenil
 m/z 173 (quantitation); m/z 175, 189 (confirmation) for BAM

Results

The results are summarized in Table B.5.3.

Acceptability

The study is considered acceptable for the overall evaluation.

VI) Analytical method for residues in water– Dichlobenil and BAM, groundwater, GC-MS, ILV**Characteristics**

Reference	: Bacher, 2004	Test substance	: Dichlobenil, batch no. ARS-9108-BA-B
Year of execution	: 2004		: 2,6-dichlorobenzamide (BAM), batch no. ARS81C25N
Guideline	: SANCO/825/00 rev. 6, 20/06/00	Purity	: Dichlobenil: 100%
GLP	: yes	Acceptable	: 2,6-dichlorobenzamide: 100%
			yes

Study design

An Independent Laboratory Validation (ILV) is performed of a GC-MS method (method no. GRL-GM-1197) for the determination of Dichlobenil and 2,6-dichlorobenzamide (BAM) in groundwater, using 2,4,6-trichlorobenzonitrile as internal standard.

The method comprises the following steps:

- solid phase extraction of sample material (1 L) on a divinylbenzene (DVB) disk (Speeddisk™)
- elution with dichloromethane, using toluene as keeper solvent
- analysis of an aliquot by GC-MS.

The analysis was performed under the following conditions:

Column:	Varian CP Sil (50% phenyl- 50% dimethylpolysiloxane), 0.25 µm film, 30 m x 0.32 mm (i.d.)
Temperature	Column: 250°C, injection: 220°C
Carrier gas:	Helium at 10 psi
MS interface:	Not indicated
Fragments:	m/z 171 (quantitation); m/z 136 (confirmation) for Dichlobenil m/z 173 (quantitation); m/z 189 (confirmation) for BAM

Results

The results are summarized in Table B.5.3.

Acceptability

The study is considered acceptable for the overall evaluation.

B.5.3.3 Analytical method for residues in air

The residue definition for monitoring in air is the parent compound Dichlobenil only.

In air the LOQ must not exceed the following concentration (C), based on the AOEL_{inhalative}.

The AOEL_{inhalative} on the other hand is based on the semi-chronic AOEL_{systemic} for Dichlobenil of 0.005 mg/kg bw/day (see B.6). Considering a 100% uptake via inhalation, the AOEL_{inhalative} is 0.005 mg/kg bw/day for Dichlobenil.

- AOEL_{inhalative} = 0.005 mg/kg bw/d Dichlobenil
- $C = (AOEL_{inhalative} \cdot 0.1 \cdot 60) / 20 = 0.0015 \text{ mg/m}^3 \text{ air.}$

Characteristics

Reference	: Bacher, 2002b	Test substance	: Dichlobenil, batch no. ARS-9108-BA
Year of execution	: 2004	Purity	: 100%
Guideline	: SANCO/825/00 rev. 6, 20/06/00		
GLP	: yes	Acceptable	: yes

Study design

Method

Air containing dichlobenil at ambient temperature and normal humidity (25°C, 26% rel. humidity) as well as warm humid air (35°C, 93% relative humidity) were sucked through adsorption tubes filled with two portions of XAD-2 porous polymer for 6 hours. The air flow accounted for ca. 1,5 L/min for the ambient air and -because of the volatility of the analyte- for 0.8 L/min for the warm, humid air.

The adsorber material was extracted with ethyl acetate followed by GC-ECD

The conditions for the analysis by GC-ECD were:

Detector:	Electron capture detector (ECD)
Column:	Chrompack CP Sil 8 CB Low Bleed fused silica, 0.25 µm film, 30 m x 0.32 mm (i.d.)
Temperature	Column: 270°C, injection: 230°C, detector: 162°C
Carrier gas:	Helium at 15 psi constant pressure

The specificity of the method was confirmed by GC-MS and GC-MS/MS.

Fragments:	m/z 171 (quantitation); m/z 173 (confirmation) and m/z 171 → 136 confirmation for Dichlobenil (MS/MS)
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Validation procedure

Absorber tubes were spiked with stock solutions in ethyl acetate straight on the absorber material. The two fortification levels were chosen to account for an average C_{air} of ca. 0.75 µg/m³ and 15 µg/m³. Extraction efficacy was determined directly. For the determination of recovery and breakthrough, conditioned air was lead through the adsorber tube for 6 hours before extraction of the fortified adsorber material (recovery) the adjacent, not fortified adsorber material, respectively.

Results

The results are summarized in Table B.5.3.

Acceptability

The study is considered acceptable for the overall evaluation.

Table B.5.3: Summary of method description and validation for Dichlobenil and its metabolite 2, 6-dichlorobenzamide (BAM) in environmental samples

Matrix	Analyte	Dissolution/ extraction	Portion/ clean-up	Quantification	Recovery fortification level	Recovery range % (mean) [overall mean]	Repeatability RSD (%) (n) [overall RSD]	Limit of Quantification	Linearity (r^2)	Reference
SOIL										
Soil (loamy sand, LUFA Speyer standard soil 2.2)	Dichlobenil	0.2% NH ₄ Cl aqueous solution/ acetone/ petroleum ether (17/75/ 75, v/v/v)	Petroleum ether/ alumina cartridge	GC-ECD	0.01 mg/kg	75 – 105 (89)	14 (5)	0.01 mg/kg	0.9969	Bacher, 2002a
					0.1 mg/kg	70 – 96 (82)	12 (5)			
Soil (loamy sand, LUFA Speyer standard soil 2.2)	BAM	0.2% NH ₄ Cl aqueous solution/ acetone/ petroleum ether (17/75/ 75, v/v/v)	Ethyl acetate/ alumina cartridge	GC-ECD	0.01 mg/kg	72 – 87 (79)	8 (4 ¹⁾) [13]	0.01 mg/kg	0.9959	Bacher, 2002a
					0.1 mg/kg	73 – 83 (78)	5 (4 ¹⁾)			
SOIL - Confirmatory method										
Soil (loamy sand, LUFA Speyer standard soil 2.2)	Dichlobenil	0.2% NH ₄ Cl aqueous solution/ acetone/ petroleum ether (17/75/ 75, v/v/v)	Petroleum ether/ alumina cartridge	GC-MS (confirmatory method)	0.01 mg/kg	89	n.a. (1)	-	0.9997	Bacher, 2002a
					0.1 mg/kg	87	n.a. (1)			
Soil (loamy sand, LUFA Speyer standard soil 2.2)	Dichlobenil	0.2% NH ₄ Cl aqueous solution/ acetone/ petroleum ether (17/75/ 75, v/v/v)	Petroleum ether/ alumina cartridge	GC-MS-MS (confirmatory method)	0.01 mg/kg	81	n.a. (1)	-	0.9997	Bacher, 2002a
					0.1 mg/kg	82	n.a. (1)			
Soil (loamy sand, LUFA Speyer standard soil 2.2)	BAM	0.2% NH ₄ Cl aqueous solution/ acetone/ petroleum ether (17/75/ 75, v/v/v)	Ethyl acetate/ alumina cartridge	GC-MS (confirmatory method)	0.01 mg/kg	72 – 115 (90)	20 (4 ¹⁾)	0.01 mg/kg	1.0000	Bacher, 2002a
					0.1 mg/kg	67 – 81 (73)	9 (4 ¹⁾)			

n.a. not applied/not applicable

1) one sample excluded as Dixon outlier

2) two sets of 5 samples were measured

Matrix	Analyte	Dissolution/ extraction	Portion/ clean-up	Quantification	Recovery fortification level	Recovery range % (mean) [overall mean]	Repeatability RSD (%) (n) [overall RSD]	Limit of Quantification	Linearity (r ²)	Reference
WATER										
Surface water (pond Preston Hill, USA)	Dichlobenil	SPE (DVB speed disk)	-	GC-MS	0.1 µg/L	82–112 (94) ¹⁾ 79–90 (86) [90]	12 (5) 5.0 (5) [10]	0.1 µg/L	0.9975	Carter, 2000
					1.0 µg/L	88–96 (93) ²⁾ 93–99 (96) [94]	3.4 (5) 2.3 (5) [3.0]			
Surface water (pond Preston Hill, USA)	BAM	SPE (DVB speed disk)	-	GC-MS	0.1 µg/L	88–106 (95) ²⁾ 97–112 (106) [101]	8.1 (5) 5.5 (5) [8.5]	0.1 µg/L	0.9985	Carter, 2000
					1.0 µg/L	83–98 (91) ¹²⁾ 91–101 (95) [93]	6.7 (5) 4.2 (5) [5.9]			
Groundwater (well Easton, USA)	Dichlobenil	-	-	HPLC-UV	0.2 mg/L	100–104 (101)	1.5 (5)	-	0.9996	Kendall and Nixon, 2003 ³⁾
					1 mg/L 10 mg/L	100–108 (104) 100–101 (100) [102]	2.8 (5) 0.57 (5) [2.2]			[No 10xLOQ level measured]
Groundwater (Lunschooten, The Netherlands)	Dichlobenil	SPE (DVB speed disk)	-	GC-MS	0.05 µg/L 0.5 µg/L	72–113 ³⁾ (93) 78–102 ³⁾ (90) [92]	20 (5) 11 (5) [16]	-	0.9976	Wyma- Teitsma, 2003 [recovery rate too high]
					0.1 µg/L 1.0 µg/L 5.0 µg/L	91–101 (96) 97–102 (99) 91–96 (94)	3.9 (5) 2.3 (5) 1.9 (5)	0.1 µg/L	1.0000	Yu, 2004
Groundwater (well water, no further information)	Dichlobenil	SPE (DVB speed disk)	-	GC-MS	0.1 µg/L	102–110 (106)	2.8 (5)	0.1 µg/L	0.9998	Yu, 2004
					1.0 µg/L 5.0 µg/L	69–96 (84) 83–89 (86)	14 (5) 2.6 (5)			

n.a. not applied/not applicable

1) one sample excluded as Dixon outlier

2) two sets of 5 samples were measured

3) recoveries are corrected for the blank, since relevant levels (0.023 µg/L) were found there – see paragraph “Acceptability” of the study summary report that reference.

4) level corresponds to 0.8 µg/m³5) level corresponds to 16 µg/m³

Matrix	Analyte	Dissolution/ extraction	Portion/ clean-up	Quantification	Recovery fortification level	Recovery range % (mean) [overall mean]	Repeatability RSD (%) (n) [overall RSD]	Limit of Quantification	Linearity (r ²)	Reference
WATER - ILV										
Surface water (pond Arcata, California, USA)	Dichlobenil	SPE (DVB speed disk)		GC-MS	0.1 µg/L	78 – 91 (83)	6.1 (5)	0.1 µg/L	1.0000	Noon, 2001
Surface water (pond Arcata, California, USA)	BAM	SPE (DVB speed disk)	-	GC-MS	1.0 µg/L	84 – 89 (87) [85]	2.5 (5) [4.8]	0.1 µg/L	1.0000	Noon, 2001
Groundwater (well water, no further information)	Dichlobenil	SPE (DVB speed disk)	-	GC-MS	0.1 µg/L 1.0 µg/L 5.0 µg/L	74 – 86 (82) 78 – 88 (84) 83 – 108 (93) 71 – 92 (86) 83 – 91 (87) [83] [89]	6.0 (5) 4.9 (5) 10 (6) 10 (5) 4 (5) [9]	0.1 µg/L	0.9994	Bacher, 2004
Groundwater (well water, no further information)	BAM	SPE (DVB speed disk)	-	GC-MS	0.1 µg/L 1.0 µg/L 5.0 µg/L	87 – 120 (100) 81 – 105 (96) 87 – 101 (93) [96]	12 (6) 10 (5) 6 (5) [10]	0.1 µg/L	0.9991	Bacher, 2004
AIR										
Ambient air	Dichlobenil	ethyl acetate	-	GC-ECD	0.4 µg ⁴⁾ 8.0 µg ⁵⁾	80 – 91 (85) 80 – 99 (88) break through: <10% [86]	5 (5) 8 (5) [7]	0.8 µg/m ³	0.9996	Bacher, 2002b
Warm humid air	Dichlobenil	ethyl acetate	-	GC-ECD	0.2 µg ⁴⁾ 4.0 µg ⁵⁾	67 – 90 (81) 73 – 81 (77) break through: <10% [79]	12 (5) 5 (5) [9]	0.8 µg/m ³	0.9996	Bacher, 2002b

n.a. not applied/not applicable

1) one sample excluded as Dixon outlier

2) two sets of 5 samples were measured

3) recoveries are corrected for the blank, since relevant levels (0.023 µg/L) were found there – see paragraph “Acceptability” of the study summary report that reference.

4) level corresponds to 0.8 µg/m³5) level corresponds to 16 µg/m³

B.5.4 ANALYTICAL METHODS (RESIDUE) FOR BODY FLUIDS AND TISSUES (ANNEX IIA 4.2.5; ANNEX IIIA 5.2)

No methods submitted.

Since the active substance Dichlobenil and its main metabolite 2,6-dichlorobenzamide are not classified as toxic or highly toxic, analytical methods for the residue determination in body fluids and tissues have not to be submitted.

B.5.5 EVALUATION AND ASSESSMENT

A collaboratively validated CIPAC method is available for the determination of Dichlobenil in Dichlobenil technical as well as in a granular formulation (CIPAC method Dichlobenil 73, Henriët et al., 1983).

Furthermore, a validated GC-FID method for the determination of 2,6-dichlorobenzonitrile in Dichlobenil technical (van Zeijl, 2003a) and a GC-FID-method for the determination of Dichlobenil in its granular formulation Casoron G (Brown, 2004) are available.

An analytical method for the determination of impurities in Dichlobenil technical is submitted as well (van Zeijl, 2003b). Since it is confidential information, the analytical method of the specified impurities is summarised in Volume 4 Annex C.

Various study reports on the validation of analytical methods for the determination of Dichlobenil and/or 2,6-dichlorobenzamide (BAM) in plant (products) are submitted.

First of all the applicability of different multi-residue methods (MRM) was investigated: FDA method for the determination of 2,6-dichlorobenzamide in apples and hazelnut (Pouwelse and van Loo, 1992), DFG method S 19 for the determination of 2,6-dichlorobenzamide in grape (Specht, 1991a) and DFG method S 19 for the determination of 2,6-dichlorobenzamide in apple (Specht, 1991b).

DFG method S19 is suitable for the determination of 2, 6-dichlorobenzamide (BAM) in grape and apple, an ILV is however not submitted.

Furthermore, one handbook reference (van Rossum et al., 1978) and three study reports on method validation are submitted (van Balkom, 1993; Brereton, 2000; Bacher, 2005) and one method validation was part of a processing study (Maselli, 1998).

The methods supplied cover next to the determination of BAM in apples also the determination of Dichlobenil and its metabolite BAM in grapes, the residue definition in the commodity of the intended use.

All determinations are based on the same principle:

- extraction of the homogenised samples with ethyl acetate (for determination of BAM) or with 20% ethyl acetate in hexane (for determination of Dichlobenil),
- clean-up of the extract with or column chromatography on alumina or in one study (Brereton, 2000) with gel permeation chromatography,

- measurement, applying GC-ECD; in one study (Bacher, 2005) also GC-MS/MS.

The handbook method description (van Rossum et al., 1978) did not contain any validation data. The information submitted in the studies of Maselli (1998), van Balkom (1993) and Brereton (2000) is not in accordance with the guideline to allow the derivation of an LOQ, since all studies have shortcomings regarding their performance and/or documentation.

Only the study of Bacher (2005) does fulfil the requirements of guideline SANCO/825/00. The LOQs of the described GC-ECD and GS-MS/MS method for the determination of both Dichlobenil and BAM in grapes account in all cases for 0.01 mg/kg. An ILV (Wolf, 2006) has also been submitted.

The notifier submitted no analytical method for products of animal origin.

Since relevant intake levels (>0.1 mg/kg dry feed) of the metabolite BAM, the component of the residue definition, occur for cattle (see B.15.1), additional data on metabolism are requested, possibly followed by the performance of a feed intake study. In case significant residues (≥ 0.01 mg/kg) occur in any edible part of the animal after intake of relevant residue (levels), appropriate validated analytical method(s) must be submitted as well.

For soil samples, a validated GC-ECD method is available for the determination of the parent Dichlobenil and its metabolite 2,6-dichlorobenzamide, which comprise together the residue definition in soil at the current intended use (Bacher, 2002a). As confirmatory methods GC-MS (for Dichlobenil and BAM) and GC-MS/MS (only for Dichlobenil) were applied. The LOQ of the GC-ECD method accounts for 0.01 mg/kg soil for both, Dichlobenil as well as for BAM.

The residue definition in water comprises also the parent compound Dichlobenil and its metabolite 2,6-dichlorobenzamide (BAM). One method validation report for the determination of both compounds in surface water, applying GC-MS (Carter, 2000) is submitted.

For groundwater the following analytical methods are submitted: a HPLC-UV method for the determination of Dichlobenil (Kendall and Nixon, 2003), a GC-MS method for the determination of Dichlobenil and BAM (Yu, 2004) and a GC-MS method for the determination of Dichlobenil (Wyma-Teitsma, 2003). Since in study of Wyma-Teitsma (2003) the recovery rate at the lower fortification level (0.05 µg/L) is not within the range of 70 -110% as requested in the guideline and in the study of Kendall and Nixon (2003) no validation at the 10times LOQ level was performed, the outcome of these two studies are not considered acceptable for the overall evaluation.

Furthermore, two ILVs are available for the GC-MS methods in surface water (Noon, 2001) as well as in groundwater (Bacher, 2004) for both Dichlobenil and BAM, resulting in all cases in a LOQ of 0.1 µg/L.

Therefore, the validated LOQ for both Dichlobenil and BAM accounts for 0.1 µg/L groundwater and surface water, determined by GC-MS.

This LOQ meets the requirements in view of the EU drinking water limit (LOQ has to be ≤ 0.1 µg/L) as well as the toxicity values for aquatic organisms (acute and long-term toxicity for algae, fish, invertebrates, aquatic plants), since the lowest level found account for 33 µg /L Dichlobenil (EC50_(14d))

for duck weed) and 25 µg/L for BAM (NOEC_(7d) for duck weed). Due to the specificity of the analytical method (GC-MS), no separate method validation is required.

For the determination of Dichlobenil in air a method based on GC-ECD was submitted (Bacher, 2002b). The method specificity was confirmed by GC-MS, extraction efficacy, recovery and breakthrough were determined for ambient and also warm humid air, resulting in both cases in a validated LOQ of 0.8 µg/m³ Dichlobenil.

The method is suitable for the determination of relevant levels of Dichlobenil in air since this LOQ level is sufficient regarding the requirements as set in the guideline. It is far below the calculated C-level of 15 µg/m³ air (based on a AOEL_{systemic} of 0.005 mg/kg bw/day Dichlobenil and the assumption of 100% uptake via inhalation).

B.5.6 REFERENCES RELIED ON**Section B.5 Method of analysis (Annex IIA, point 4, Annex IIIa, point 5)**

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIA, 4.1.1/01 IIA, 4.1.3/01	Zeijl, E. van	2003a	Validation of the analytical method for the determination of 2,6-dichlorobenzonitrile in dichlorobenzonitrile technical by gas chromatography and internal standardization Report no. AAL-FR-10003 CA - 4113 Date: 20-02-2003 GLP, unpublished	Y	CHEM
IIA, 4.1.1/02	Henriet, J. et al.	1983	Analytical method for technical Dichlobenil and its formulation. CIPAC Handbook Volume 1B: 1769-1773. CA – 2330 Non-GLP, published	N	-
IIA, 4.1.2/08	Bacher, R.	2005	Validation of an analytical methods for the determination of dichlobenil and its metabolite 2,6-dichlorobenzamide (BAM in grapes) Report PTRL Europe GmbH, Germany No. B962 G GLP, Unpublished	Y	CHEM
IIA, 4.1.2/08	Wolf, S.	2006	Independent laboratory validation (ILV) of analytical methods for the determination of dichlobenil and its metabolite 2,6-dichlorobenzamide (BAM) in grapes Report RCC Ltd. Switzerland, A56687 CA - 4234 GLP, Unpublished	Y	CHEM
IIA, 4.2.2/01	Bacher, R.	2002a	Validation of an analytical method for the determination of Dichlobenil and its metabolite 2,6-dichlorobenzamide (BAM) in soil by GC/ECD, demonstrating GC/MS as confirmatory method Report PTRL Europe, Germany No. B 556 G CA – 4090 GLP, Unpublished	Y	CHEM
IIA, 4.2.3/01	Carter, D.S.	2000	Analytical method for determining Dichlobenil and its metabolite 2,6-dichlorobenzamide in water Report Uniroyal Chemical Co. Inc., Middlebury, U.S.A. No.99055 CA - 3922 GLP, Unpublished	Y	CHEM
IIA, 4.2.3/05	Yu, W.S.	2004	Validation of an analytical method for the determination of Dichlobenil and 2,6-dichlorobenzamide (BAM) in groundwater Report Crompton Co., Research Laboratories, Ontario, Canada No.GRL-12141 CA – 4204 GLP, Unpublished	Y	CHEM

Annex point / reference no.	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Data protection claimed Y/N	Owner
IIA, 4.2.4	Bacher, R.	2002b	Development and validation of an analytical method for the determination of Dichlobenil in air Report PTRL Europe GmbH, Germany No.B562G CA – 4095 GLP, Unpublished	Y	CHEM
IIIA 5.1/01	Brown, M.H.	2004	Validation of a method for the determination of Dichlobenil in Casoron G Report Crompton Co., Research Laboratories, Ontario, Canada No.GRL 12181 CA – 4203 GLP, Unpublished	Y	CHEM
IIIA 5.1/01	Tutty, D. G. Riggs, A. S.	2006	Supplemental report – dichlobenil technical/Casoron G Report Chemtura Canada Co., Guelph Technology Centre, Canada, 155802/160/2006 non-GLP, Unpublished	Y	CHEM
IIA, 5.1/02	Henriet, J. et al.	1983	Analytical method for technical Dichlobenil and its formulation. CIPAC Handbook Volume 1B: 1769, 1773. CA – 2330 Non-GLP, published	N	-